SPECTRUM AND OUTCOME IN ADULT PATIENTS OF SUBACUTE AND CHRONIC MENINGITIS

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I hereby declare that the thesis entitled **"SPECTRUM AND OUTCOME IN ADULT PATIENTS OF SUBACUTE AND CHRONIC MENINGITIS**" submitted towards partial fulfilment of the requirements for the award of **MD in GENERAL MEDICINE** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Gautam Ahluwalia**, Professor, Department of Medicine, **Dr. Gagandeep Singh**, Professor & Head, Department of Neurology and **Dr. Pavneet Kaur Selhi**, Professor Department of Pathology, DMCH Ludhiana No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

My Family

Friends

and

Teachers

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LIST OF ABBREVIATIONS

ADA	Adenosine deaminase
AFB	Acid fast bacilli
AIDS	Acquired immunodeficiency syndrome
ATT	Anti tubercular therapy
CBNAAT	Cartridge based nucleic acid amplification test
CM	Chronic Meningitis
CNS	Central nervous system
CSF	Cerebrospinal fluid
CT	Computed tomography
DAMA	Discharge against medical advice
DOR	Discharge on request
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HSV	Herpes Simplex Virus
IGRA	Interferon gamma release assay
LPA	Line probe assay
MRI	Magnetic resonance imaging
NAAT	Nucleic acid amplification test
PCR	Polymerase chain reaction

PTB	Pulmonary tuberculosis
SAM	Subacute meningitis
TB	Tuberculosis
TBM	Tubercular meningitis
TST	Tuberculin skin test
VDRL	Venereal disease research laboratory
VZV	Varicella Zoster Virus

ABSTRACT

INTRODUCTION- Meningitis is defined as inflammation involving the meninges of the brain and spinal cord. Meningitis can be categorized as acute, subacute, or chronic based on duration of inflammation. Chronic meningitis affects about 10% of patients diagnosed with meningitis.

AIMS & OBJECTIVES- To study the spectrum and outcome of admitted adult patients aged > 18 years with subacute and chronic meningitis.

MATERIAL & METHODS- A prospective study was conducted on patients aged more than 18 years admitted with subacute and chronic meningitis in Department of Medicine and allied Specialities of Dayanand Medical College and Hospital (DMCH), Ludhiana from 1st March 2021 to 28th February 2022 and they were statistically analysed.

CLINICAL SIGNIFICANCE- Subacute meningitis (SAM) is commonly defined as inflammation evolving for greater than 5 days and less than 30 days and chronic meningitis (CM) as greater than 30 days without resolution of cerebrospinal fluid (CSF) abnormalities.This study is aimed at delineating the etiology, clinical spectrum and outcome of subacute and chronic meningitis in patients admitted in a tertiary care teaching hospital.

RESULTS- Out of 55 patients studied, SAM (83.6%) was more common than CM (16.4%). Altered sensorium (74.5%), fever (69.1%), headache (38.2%), vomiting (40%), seizure (12%) were the most common symptoms. The most common etiologies were tubercular meningitis (81.8%), cryptococcal meningitis (10.9%), viral meningitis (7.3%) in both subacute and chronic meningitis. The mean length of stay was 12.50 days in ward and 5 days in ICU. 67.3% of patients got discharged, 18.2% were discharged on request (DOR), 14.5% were discharged against medical advice (DAMA). There had been 2 mortalities in 2 patients that could be followed after DAMA.

CONCLUSION- Due to insidious presentation, establishing a proper diagnosis and providing timely treatment for patients with subacute and chronic meningitis remains a challenge for clinicians.

KEYWORDS- Subacute meningitis (SAM), chronic meningitis (CM), cerebrospinal fluid (CSF), discharge on request (DOR), discharge against medical advice (DAMA)

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INTRODUCTION

Meningitis is a clinical syndrome characterized by inflammation of meninges. The classic triad of meningitis consists of fever, headache and neck stiffness [1] Bacterial meningitis occurs in about 3 people per 100,000 annually in western countries. Population-wide studies have shown that viral meningitis is more common at 10.9 per 100,000 [2] population.

Bacterial (pyogenic) meningitis is a pyogenic inflammation of meninges and subarachnoid cerebrospinal fluid (CSF) and is characterized by neutrophilic pleocytosis in CSF.[3] Pneumococcal meningitis is caused by *streptococcus pneumonia*, a gram-positive coccus and is the most common bacterial cause of meningitis. Meningococcal meningitis is caused by gram-negative diplococcus - *Neisseria meningitides*. Most patients recover completely if appropriate antibiotic therapy is instituted promptly.[3]

Tubercular meningitis is a very critical disease in terms of fatal outcome and permanent sequelae, requiring rapid diagnosis and treatment.[4]. Tuberculous meningitis should be a strong consideration when a patient presents with clinical picture of meningoencephalitidis, especially in high risk groups, including persons with malnutrition, those with alcohol abuse or drug abuse and patients with known retroviral infection. Death may occur as a result of missed diagnosis and delayed treatment.[5] World-wide causes of viral meningitis include *enterovirus, herpes, mumps, measles* and *HIV*. *Enterovirus* is the most common cause of viral meningitis.

Aseptic meningitis is an illness characterized by serious inflammation of the meninges, usually with an accompanying CSF lymphocyte pleocytosis. Clinical manifestations vary with headache and fever predominating. The illness is usually mild and runs its course without treatment, however some cases can be severe and life threatening.

Remarkable recovery may be achieved in some patients with viral meningitis who become even comatosed. Vigorous supportive therapy and avoidance of complications are very important in managing these patients.[6]

Cryptococcal meningitis is caused by the yeast *Cryptococcus neoformans*, especially in persons with defective cell mediated immunity. Prompt antifungal therapy should be considered in these patients.[7]

The incidence of acute encephalitis in western countries is 7.4 per 100,000 population per year. In tropical countries like India it is 6.4 per 100,000 per year. Herpes simplex encephalitis has an incidence of 2-4 per million population per year.

Encephalitis presents as diffuse or focal neuropsychological dysfunction although it primarily involves the brain, it often involves the meninges as well (meningoencephalitis). From an epidemiologic and pathophysiologic perspective encephalitis is distinct from meningitis, though on clinical evaluation both can be present, with signs and symptoms of meningeal inflammation. The prodrome typically consists of fever, headache, nausea, vomiting, lethargy and myalgias. The clinical presentation is encephalopathy with diffuse or focal neurological symptoms including behavioural and personality changes, with decreased level of consciousness, neck pain/stiffness, photophobia,lethargy, generalized or focal seizures, acute confusion or amnestic states and flaccid paralysis.[8]

This study is done to emphasize the importance of early diagnosis, so that prompt management is given at appropriate time.

Meningitis can be categorized as acute, subacute, or chronic based on duration of inflammation. Subacute meningitis (SAM) is commonly defined as inflammation evolving for greater than 5 days and less than 30 days and chronic meningitis (CM) as greater than 30 days without resolution of cerebrospinal fluid (CSF) abnormalities. Most organisms causing acute meningitis rarely persist more than a few weeks.[5] Patients

with chronic meningitis usually have a subacute onset of symptoms including fever, headache, and vomiting. The symptoms can remain static, fluctuate, and/or slowly worsen. The symptoms and clinical course of chronic meningitis vary widely from patient to patient.

Chronic meningitis affects about 10% of patients diagnosed with meningitis.[6] Some individuals with chronic meningitis seek medical attention before the symptoms or signs have been present for 4 weeks, so it is important to differentiate these patients from those who are recovering from acute or recurrent meningitis.[8]

In our country, there is a paucity of epidemiological data about subacute and chronic meningitis, especially in admitted patients. This study is aimed at delineating the etiology and clinical spectrum of subacute and chronic meningitis in adult patients admitted in a tertiary care teaching hospital.

AIMS AND OBJECTIVES

- To study the spectrum of admitted adult patients aged > 18 years with subacute and chronic meningitis.
- To study the outcome in these patients, wherever feasible

REVIEW OF LITERATURE

Meningitis is defined as the inflammatory process of the membranes that surround the brain and spinal cord. Meningitis is also referred to as arachnoiditis or leptomeningitis. Meningitis affects the arachnoid, pia and CSF.

When the meninges, the subarachnoid space, and the brain parenchyma are all frequently involved in the inflammatory reaction, it is defined as meningoencephalitis.

Zunt et al suggested that meningitis can be categorized as acute, subacute, or chronic based on duration of inflammation. Community acquired meningitis can be classified as acute or subacute based on the duration of symptoms of < 5 or >5 days. Chronic meningitis is commonly defined as inflammation evolving during weeks to months without resolution of CSF abnormalities. Determining the time course of meningitis is important for creating a differential diagnosis. Although numerous etiologies of subacute and chronic meningitis have been identified, the most common etiologies are: (1) infectious, (2) autoimmune, and (3) neoplastic.[4]

Ginsberg et al suggested that meningitis is a clinical syndrome characterized by inflammation of meninges. The classic triad of meningitis consists of fever, headache and neck stiffness.[5] Bacterial meningitis occurs in about 3 people per 100,000 annually in western countries. Population-wide studies have shown that viral meningitis is more common at 10.9 per 100,000[6] population.

Meningitis was initially recognized in the early 1800's. Even until the beginning of 20th century bacterial meningitis was nearly 90% fatal. This shows that the disease is most virulent and causes a great deal of mortality and morbidity. The advent of the antibiotics in the beginning of the twentieth century brought a cure to meningitis. Inspite of antibiotics

the sequelae of meningitis after completion of treatment is a great burden to the society.[7]

Meningitis, a major neurological emergency, is inflammation of any of the three meningeal layers. Meningitis is classified into acute, subacute,and chronic meningitis based on symptoms duration of <5 days, ≥5 days and ≥4 weeks, respectively. Chronic meningitis occurs rarely and accounts for almost 10% of all meningitis patients. [5,9,10,11] To date, several etiologies have been identified for meningitis. The etiologies differ in acute meningitis compared to subacute and chronic meningitis. Community-acquired bacteria and viruses tend to cause acute meningitis, whereas atypical indolent bacteria (mainly *Mycobacterium tuberculosis*), fungi(predominantly *Cryptococcus neoformans*), and non-infectious etiologies cause subacute and chronic meningitis. [4,11,12,13] Subacute meningitis has less bacterial etiologies and more fungal causes compared to acute meningitis. Also, subacute and chronic meningitis present with lower cerebrospinal fluid (CSF) white blood cells (WBC) count and higher rate of decreased CSF glucose in comparison with acute meningitis. Chronic meningitis tends to have milder symptoms compared to acute meningitis. [11,13]

Characteristics of the immune system, socioeconomic status, location, travel history, medical history, and medications are factors that influence the prevalence and the emergence of symptoms. [14,15] The patient's history and physical examination are of most value in the diagnosis of chronic meningitis. The most typical symptoms are headache, nausea, vomiting, and cranial nerve neuropathies. Other factors affecting the patient, including past medical history, medication history, intravenous drug use, sexual history, and recent travel history, must be considered when compiling a medical history. Regarding physical examination, we have to search for any skin lesions, ophthalmologic signs, signs of pulmonary infections. A thorough and precise neurologic examination is required. [16,17] The next step is to perform radiology tests and CSF

analysis for CSF glucose level, WBC count, and protein level. The most prevalent findings of CSF analysis are lymphocytic pleocytosis, elevated protein level, and normal or decreased glucose. Ventriculitis, diffuse leptomeningeal enhancement, hydrocephalous, and cranial nerve enhancement are significant findings on magnetic resonance imaging (MRI) with gadolinium contrast. [4,18] Finally, when a definitive diagnosis is not possible, a biopsy is performed to confirm the diagnosis. [19] Aside from the evaluations and diagnostic tests, teamwork, and collaboration between specialists in infectious disease, neurology, radiology, ophthalmology, and rheumatology is essential to reach an appropriate conclusion. [16]

Accurate and timely diagnosis of chronic meningitis and its etiologies have remained a challenge because of broad range of etiologies, including infectious, autoimmune, and neoplastic diseases, which are difficult to differentiate. [20]

Tubercular meningitis is a very critical disease in terms of fatal outcome and permanent sequelae, requiring rapid diagnosis and treatment.[21] Tuberculous meningitis should be a strong consideration when a patient presents with clinical picture of meningoencephalitis, especially in high-risk groups, including persons with malnutrition, those with alcohol or drug abuse and patients with known retroviral infection. Deathmay occur as a result of missed diagnosis and delayed treatment.[22]

Two commonly used methods -Thwaites' scoring system (Table 1)[23] and more recently, the Lancet consensus scoring system (Table 2) havebeen developed to help determine the probability of TBM and to help clinicians determine if TBM should be suspected and empirically treated.[24] The scoring systems include clinical features, CSF findings, as well as neurological imaging in making a diagnosis. This study was designed to explore the diagnostic utility of the "Thwaites' system" and "Lancet consensus scoring system" in differentiating TBM from the other more common etiologies of SAM where TBM is an important consideration.

Table 1: Thwaites scoring system	
Parameters	**Score**
Age (Years)	
≥ 36	2
< 36	0
WBC (10^3 /ml)	
≥ 15,000	4
< 15,000	0
History of illness (days)	
≥ 6	5
< 6	0
CSF total WBC (10^3 /ml)	
≥ 900	3
< 900	0
CSF % neutrophils	
≥ 75	4
< 75	0

Table 2: Lancet scoring system	
Clinical criteria	**(Maximum Category Score = 6)**
Symptom duration of more than 5 days	4
Systemic symptoms suggestive of tuberculosis (one or more of the following): weight loss (or poor weight gain in children), night sweats, or persistent cough for more than 2 weeks	2
History of recent (within past year) close contact with an individual with pulmonary tuberculosis or a positive TST or IGRA (only in children < 10 years of age)	2
Focal neurological deficit (excluding cranial nerve palsies)	1
Cranial nerve palsy	1
Altered consciousness	1
CSF Criteria	**(Maximum category score = 4)**
Clear appearance	1
Cells: 10–500 per µl	1
Lymphocytic predominance (> 50%)	1
Protein concentration greater than 1 g/L	1
CSF to plasma glucose ratio of less than 50% or an absolute CSF glucose concentration less than 2.2 mmol/L	1
Cerebral imaging criteria	**(Maximum category score = 6)**
Hydrocephalus	1
Basal meningeal enhancement	2
Tuberculoma	2
Infarct	1
Pre-contrast basal hyperdensity	2
Evidence of tuberculosis elsewhere	**(Maximum category score = 4)**
Chest Radiograph suggestive of active TB: signs of TB = 2; miliary TB = 4	2/4
CT/ MRI/ ultrasound evidence for tuberculosis outside the CNS	2
AFB identified or *Mycobacterium tuberculosis* cultured from another source— i.e. sputum lymph node, gastric washing, urine, blood culture	4
Positive commercial *M. tuberculosis* NAAT from extra-neural specimen	4

Exclusion of alternative diagnosis

An alternative diagnosis must be confirmed microbiologically (by stain, culture, or NAAT when appropriate), serologically (e.g., syphilis), or histopathologically (e.g., lymphoma). The list of alternative diagnosis that should be considered, dependent upon age, immune status, and geographical region, include: pyogenic bacterial meningitis, cryptococcal meningitis, syphilitic meningitis, viral meningo-encephalitis, cerebral malaria, parasitic or eosinophilic meningitis (*Angiostrongylus cantonesis, Gnathostomaspinigerum, toxocariasis, cysticercosis*), cerebral toxoplasmosis and bacterial brain abscess (space-occupying lesion on cerebral imaging) and malignancy (e.g. lymphoma)

Tuberculin skin test (TST), Interferon-gamma release assay (IGRA), Nucleic acid amplification test (NAAT), Acid-fast bacilli (AFB). The individual points for each criterion (one, two, or four points) were determined by consensus and by considering their quantified diagnostic value as defined in studies.

The “Thwaites’ system” and “Lancet consensus scoring system” showed poor diagnostic accuracy to distinguish TBM from other causes of SAM and CM. Other etiologies should be considered especially in patients with possible TBM by Lancet criteria. Novel CSF molecular diagnostic methods may increase the yield to identify the etiologies and ultimately improve care.[1]

ETIOLOGY OF MENINGITIS

Infectious Causes

Viral

DNA viruses: *HSV1, HSV2, HHV6, Ebstein Barr Virus, Varicella Zoster Virus, Cytomegalovirus, Adeno virus – serotypes 1, 6, 7, 12, 32.*

RNA viruses: *Influenza virus A, enterovirus, arboviruses like Japanese B encephalitis, West Nile Virus and retrovirus like HIV.*

Bacterial

Streptococcus pneumoniae, Neisseria meningitidis, Listeria monocytogenes, Hemophilus influenza, Escherichia coli, leptospira, legionella, Salmonella typhi, Rickettsia typhi (endemic typhus), Rickettsia prowazekii (epidemic typhus)

Fungal

Cryptococcosis, histoplasmosis, Blastomyces, Candidiasis, Coccidiosis, Aspergillosis and Mucormycosis

Parasitic

Plasmodium, Toxoplasma gondii, Naegleria fowleri, Schistosomiasis.

Non infectious causes

Drugs

Non-steroidal anti-inflammatory drugs (NSAIDs), Trimethoprim sulfamethoxazole, Amoxicillin, Azathioprine, IV Immunoglobulin, Isoniazid, Intrathecal methotrexate, Intrathecal cytosine arabinoside, Allopurinol, Carbamazepine, Sulfasalazine

Systemic diseases

Collagen vascular disorders, Systemic lupus erythematosus, Wegener

granulomatosis, Central nervous system vasculitis, Rheumatoid arthritis, Kawasaki disease, Sarcoidosis, Leptomeningeal cancer, Behcet disease, Vogt Koyanagi syndrome.

Neoplastic disorders

Leukemia, Carcinomatous meningitis secondary to primary or secondary tumors of brain.

Inflammation of neighbouring structures

Brain abscess, Epidural abscess

Miscellaneous

Arachnoiditis, Migraine, Urinary tract infection

BACTERIAL MENINGITIS

Bacterial meningitis is an inflammation of the meninges, in particular the arachnoid and the pia mater, associated with the invasion of bacteria into the subarachnoid space, principles known for more than 100 years.[25] The pathogens take advantage of the specific features of the immune system in the CNS, replicate and induce inflammation.[26] A hallmark of bacterial meningitis is the recruitment of highly activated leukocytes into the CSF. *Streptococcus pneumoniae* and *Neisseria meningitidis* are the most common and most aggressive pathogens of meningitis. Emerging antibiotic resistance is an upcoming challenge.[27] The CSF in bacterial meningitis is characterized by a strongly elevated white blood cell count (>500 cells/µl) with predominant neutrophils and a strongly elevated protein (>1 g/l), indicating severe blood—CSF barrier disruption. Increased lactate (>0.3g/l) and decreased glucose CSF/blood ratio (<0.4) support the diagnosis of acute bacterial meningitis.[28]

VIRAL MENINGITIS

World-wide causes of viral meningitis include *enterovirus, herpes*, mumps, measles and HIV. *Enterovirus* is the most common cause of viral meningitis. Aseptic meningitis is an illness characterized by serious inflammation of the meninges, usually with an accompanying CSF

lymphocyte pleocytosis. The most common viruses causing aseptic meningitis are the *enteroviruses* [29] which account for more than half the cases. More than 50 serotypes have been linked with meningitis. Clinical manifestations vary with headache and fever predominating. The illness is usually mild and runs its course without treatment, however some cases can be severe and life threatening. Mumps is another important cause of viral meningitis.*Herpes* viruses both type 1 (herpes labialis) and type 2 (genital herpes) can cause meningitis in children, especially infants*. Varicella Zoster Virus* can also cause meningitis but only in those who are immunocompromised. HIV may cause aseptic meningitis mostly at the time of sero conversion. It is difficult to assess the overall contribution of arbo viruses, but in epidemics a sizeable number of patients especially children will exhibit a benign illness with neurologic manifestations. This assumes special importance since Japanese encephalitis- an arboviral encephalitis is widely rampant in India. In the Central India, *Western Equine Encephalitis Virus* causes more cases of meningitis than the *Eastern Equine Encephalitis Virus*, which causes a more serious illness. The *St Louis Encephalitis Virus* may cause a meningitic picture in up to 60% of children affected. The *Lymphocytic Choriomeningitis Virus* - an arena virus, is a rare cause of aseptic meningitis. The respiratory viruses - *influenza A & B, adenoviruses* and *rhinoviruses* can occasionally cause meningitis. [30,31] Remarkable recovery may be achieved in some patients with viral meningitis who become even comatosed. Vigorous supportive therapy and avoidance of complications are very important in managing these patients.[32]

PARTIALLY TREATED BACTERIAL MENINGITIS

As the early symptoms and signs of bacterial meningitis are non-specific, up to 50% of cases may initially receive oral antibiotics. This partial treatment may delay the patient's presentation to hospital and result in a diagnostic dilemma. The CSF findings may be altered; Gram stain and growth of organism may be negative; however antibiotics rarely interfere with CSF protein or glucose. In this situation CSF should be sent for both

PCR and bacterial antigen detection, as these are not affected by prior antibiotic administration.[33]

TUBERCULOUS MENINGITIS

This remains an important cause of childhood hospital admissions, mortality and permanent disability in India. Tuberculosis produces basal meningitis thereby causing damage especially to basal structures- brain stem, cranial nerves and basal ganglia. The illness usually has a subacute onset with 3 clinical stages. In stage 1, symptoms are nonspecific with irregular fever, irritability, occasional vomiting, headache, lethargy or malaise. Stage II is characterized by appearance of meningeal signs, convulsions or neurodeficits while stage III is accompanied by coma, decerebration and persisting deficits.[34] Prognosis is closely related to the stage of the disease in which it is diagnosed and treatment is started. A high index of suspicion is therefore extremely important to prevent permanent disability. A study from Lucknow revealed 5 clinico-laboratory features which are suggestive of TBM in patients hospitalized with meningoencephalitis: a prodromal stage of >7 days, extrapyramidal signs, focal deficits, and optic atrophy and CSF pleocytosis with >50% lymphocytes.[35] TBM is a medical emergency associated with high morbidity and mortality. Early empirical treatment with ATT should be started if clinical suspicion is high. Ensuring compliance with chosen ATT regimen and supportive therapy cannot be overemphasized. Current ATT regimens are extrapolated from PTB regimens and do not consider poor CNS penetration of drugs such as ethambutol, streptomycin, and rifampicin. Improvement in social indicators of a country, namely, malnutrition, poverty, and low income will play an important role in the prevention and control of TB.[36]

LYME DISEASE

This is the most common vector borne disease in the US, caused by *Borrelia burgdorferi* - a fastidious, microaerophilic spirochete. Its prevalence in India is not known. In a study from Delhi, none of 27

patients presenting with mono/oligo arthritis of unknown etiology, 12 healthy blood bank donors, 25 patients with rheumatoid arthritis and 20 deer handlers were positive for IgG antibodies to *Borrelia burgdorferi*. [37] The illness is divided into early localised disease with a rash at the site of the tick bite often accompanied by fever, myalgia, headache and malaise; early disseminated disease with secondary erythema migrans lesions, constitutional symptoms, aseptic meningitis, cranial nerve palsies and carditis and late disease with chronic polyarthritis. Central nervous system manifestations are common in Lyme disease. Meningitis manifests several weeks after appearance of skin lesions, but while erythema migrans lesions are still present. Hypoglycorrhachia is not a prominent finding in the CSF. Facial nerve palsy, sometimes bilateral, may be observed. Diagnosis may be established by detection of specific IgM by ELISA, validated by Western Blot assay or by culturing the organism from a symptomatic patient. A study on differentiating features between Lyme meningitis and other aseptic meningitis showed that lyme meningitis should be suspected in cases of meningitis with very lowCSF neutrophilic counts and high protein levels associated with prolonged duration of symptoms, low grade fever and absence of pronounced signs of meningitis. [38]

BRUCELLOSIS

This is a systemic infection caused by a small, aerobic, non-spore bearing, nonmotile Gram negative coccobacillary bacteria, seen usuallyin persons living or working in close contact with animals, or consuming animal products such as raw milk or cheese made from raw milk. It is most common in the Mediterranean region, Asia, Africa, Mexico, South and Central America. Clinical features are extremely variable. In the acute form the illness presents with flu like illness with fever, night sweats, malaise, anorexia, headache and myalgias. In the undulant form, symptoms are again fever, arthritis and epididymoorchitis. Neurological involvement occurs in about 5% of patients. Diagnosis is confirmed by the isolation of brucella organisms from bacterial culture or increase over

time of specific antibodies in blood. A study from Bikaner (Rajasthan) revealed 92 cases of brucellosis diagnosed on the basis of a history of contact with animals, fever, arthralgia and brucella antigen in serum in a titre of 1:160 or more. Of these, 12 had neurobrucellosis, 4 aseptic meningitis,2 myelitis, 5 polyradiculoneuropathy and 1 polyradiculomyeloencephalopathy.[39]

EHRLICHIOSIS

Suspicion of *Ehrlichia* meningoencephalitis should be raised in elderly patients presenting with fever and encephalopathy in the summer season with history of tick bite or residence in wooded areas. Thrombocytopenia and transaminitis should raise further suspicion. CSF studies typically show a lymphocytic pleocytosis and elevated protein. PCR technique allows for direct detection of pathogen-specific DNA and is the preferred method of detection during the acute phase of illness. Prompt treatment with doxycycline results in good outcomes. Doxycycline is not included in the typical meningitis regimen; therefore, this disease is important to quickly identify as delay in Doxycycline can result in worse outcomes.[40]

LEPTOSPIROSIS

This is a zoonotic disease caused by the leptospiral spirochete. It may have an icteric or anicteric course. Anicteric leptospirosis usually presents as aseptic meningitis. A large epidemiological study in Kolenchery, Kerala after irrigation of dry lands picked up 976 cases of leptospirosis. The main reservoir for this zoonosis is the rat. In children and housewives, the main source of infection is a pet dog. IgM ELISA test is very sensitive though less specific for the diagnosis.[41]

SYPHILITIC MENINGITIS

Neurosyphilis can cause both symptomatic and asymptomatic meningitis. However, the epidemiology of modern neurosyphilis is not well defined because of the paucity of population-based data. The majority of neurosyphilis cases have been reported in HIV-infected

patients. Syphilis presenting with a skin rash and an extremely high RPR titer could indicate CNS infection rather than simply secondary syphilis because rash is a nonspecific manifestation of disseminated infection.[42] Because of a lack of typical clinical presentation, CSF VDRL test should always be included in the diagnostic work up of aseptic meningitis.

FUNGAL MENINGITIS

Meningeal involvement can occur as the most serious manifestation of disseminated fungal infections. This occurs primarily in patients with AIDS, after organ transplantation, on immunosuppressive therapy or long-term steroids. However, the most common fungal pathogen, *Cryptococcus neoformans* can occur in immunocompetent patients. Prompt antifungal therapy should be considered in these patients. [43] Subacute or chronic meningitis is the most common clinical manifestation of disseminated cryptococcosis. Cryptococcal antigen assay in the CSF may be helpful in diagnosis

Distinguishing the etiologies also helps in terms of both reducing antibiotic usage and hospital bed occupancy and reassuring contacts of cases and health care staff of a non-bacterial causes. This study is done to emphasize the importance of early diagnosis, so that prompt management is given at appropriate time.

MATERIALS AND METHODS

SOURCE OF DATA

All the patients aged more than 18 years admitted with subacute and chronic meningitis in Department of Medicine and allied Specialties of Dayanand Medical College and Hospital (DMCH), Ludhiana.

METHOD OF COLLECTION OF DATA

Study Population

A prospective observational study was conducted in adult patients hospitalized with subacute and chronic meningitis in DMCH, Ludhiana. This study duration was from 1st March 2021 to 28th February 2022.

Inclusion Criteria

- Age $\geq$ 18 years.
- Patients with symptoms of subacute and chronic meningitis admitted in department of Medicine and allied specialties.
- Duration of symptoms more than 5 days
- CSF White cell count > 5 cells/mm^3

Exclusion Criteria

- Age < 18 years.
- Previous history of trauma or with cerebrospinal fluid leak or any previous history of neurosurgery.
- Patients not giving consent for enrollment in the study.

DIAGNOSIS

CSF evaluation is the single most important aspect of the laboratory diagnosis of meningitis.

Basic studies of CSF that were performed in all patients with meningitis included measurement of cell count and white cell differential; determination of glucose and protein levels; Gram's stain and culture, CBNAAT, ADA, cryptococcal antigen.

VIRAL MENINGITIS -CSF mononuclear pleocytosis with normal to elevated CSF proteins with positive Polymerase chain reaction (PCR) test for viruses like *enterovirus*, *Varicella Zoster Virus (VZV)* and *Herpes Simplex Virus (HSV).*[44]

TUBERCULOUS MENINGITIS-Certain clinical characteristics such as longer duration of symptoms (>six days), moderate CSF pleocytosis, and the presence of focal deficits increase the probability of TBM [45,46]. Characteristic CSF findings of TBM include the following.[47]

(i) lymphocytic-predominant pleocytosis. Total white cell counts are usually between 100 and 500 cells/μL.

(ii) elevated protein levels, typically between 100 and 500 mg/dL

(iii) low glucose, usually less than 45 mg/dL or CSF: plasma ratio<0.5.

(iv) ADA >10U/L [48]

(v) CSF CBNAAT positive

FUNGAL MENINGITIS- lymphocytic or monocytic pleocytosis with elevated proteins with positive CSF Indian Ink or positive CSF Cryptococcal antigen.[49]

OUTCOME

- Diagnosis at time of discharge / discharge on request (DOR) / death / discharge against medical advice (DAMA).
- Length of stay in hospital.
- Clinical/laboratory/treatment profile of admitted patients.
- Details of pre admission workup and treatment outside (wherever available)
- Follow-up post-discharge (wherever feasible) Months: 2 and 4

Statistical Analysis:

The data was analyzed statistically using appropriate methodology. Data was described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations were done using SPSS (Statistical Package for the Social Science) 21 version statistical program for Microsoft Windows.

DID THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Investigations considered necessary by the treating unit/department were evaluated. The investigations were broadly divided into the following groups:

- Basic investigations: CBC, LFT, RFT, Urine routine, inflammatory markers like ESR
- Specific investigations: cerebrospinal fluid analysis - biochemical and/or cytopathological analysis and/or nucleic acid amplification test and/or gram stain and/or culture and/or India ink and/or viral markers and/or autoimmune antibodies.
- Radiological investigations: Chest X-Ray, CT scan, MRI
- Detailed proforma format is attached here with thesis

HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF ABOVE REQUIREMENTS?

Yes Attached herewith

OBSERVATION AND RESULTS

This prospective study was carried over a period of 12 months and included 55 patients admitted in the department of medicine and allied specialities.

Out of 55 patients admitted, the number of patients having duration of illness between 5-30 days were 46(83.6%) and with duration of illness > 30 days were 9 patients (16.4%) (table 3, figure1). The common etiologies were tubercular Meningitis in 45 (81.8%) patients followed by cryptococcal Meningitis in 6(10.9%) patients and viral Meningitis in 4 (7.3%) patients. 37 cases of tubercular meningitis (82.2%), 5 cases of cryptococcal meningitis (83.3%), 4 cases of viral meningitis (100%) were subacute. 8 cases of tubercular meningitis (17.8%), 1 case of cryptococcal meningitis (16.7%), were chronic with duration of illness >30 days. None of the cases of viral meningitis were chronic. (table 4, figure 2)

Out of 55 admitted patients, maximum number of patients(n=14) were in age group of <30 years with mean of 44.7 years (range 18–80 years). Subacute meningitis was more common in age group 31-40 years (n=11) (23.9%) whereas chronic meningitis was more common in age group <30 years(n=5)(55.6%)(table 5).12 cases of Tubercular meningitis were seen in age group <30 years(26.7%) followed by 11 cases seen in age group of more than 60 years(24.4%).Cryptococcal meningitis was maximum in age group 31-40 years(50%)(n=3).Viral meningitis was maximum in age group of 41-50 years(50%)(n=2)(table 6,figure 3).

Out of 55 patients admitted, 31(56.4%) were males and 24 (43.6%) were females. 23 cases of subacute meningitis were males (50%) and 23 cases were females (50%).8 cases of chronic meningitis were males (88.9%) and 1 case was female (11.1%) (table 5). All the cases of cryptococcal meningitis were seen in males (100%). There was not much difference seen in gender distribution in cases of tubercular meningitis. 21 cases were females (46.7%) and 24 were males (53.3%).

Viral meningitis was commonly seen in females(n=3) (75%) (table 6, figure 4).

The most common symptoms overall were altered sensorium in 41 (74.5%) patients, fever in 38(69.1%) patients, nausea and vomiting in 22(40.0%) patients, headache in 21 (38.2%) patients and seizure in 12(21.8%) patients. In subacute meningitis, the most common symptom was altered sensorium seen in 36 patients(78.3%) and the most common symptom in chronic meningitis was fever seen in 7 patients(77.8%)(table 7). The most common symptom in tubercular meningitis was altered sensorium(77.8%),in cryptococcal meningitis was headache(83.3%),in viral meningitis was fever(100%)(table 8,figure 5).The type of seizure in all patients was GTCS. Among patients with altered sensorium, 4 patients had significant deterioration in consciousness with Glasgow coma scale less than 10; Two patients had deep coma with GCS 3/15 throughout the hospitalization with poorly reacting pupils. Both of them were tubercular meningitis. One had extensive vasculitic infarcts in the bilateral cerebral hemisphere and brainstem; Among the remaining 3 patients, 2 patients had normal MRI and one had hydrocephalus. All these 4 patients were on ventilatory support in ICU.

The most common signs were nuchal rigidity (69.1%), cranial nerve palsy (9.1%). Nuchal rigidity was present in 35 cases of subacute meningitis (76.1%) and in 3 cases of chronic meningitis (33.3%) (table 9). MC Cranial nerve involved was 6^{th} Nerve. Out of 6 cases of cryptococcal meningitis, one patient had 6^{th} nerve palsy. Out of 45 cases of tubercular meningitis, four cases had cranial nerve involvement. Out of these four, three patients had 6^{th} nerve involvement and one patient had facial nerve involvement (table 10,figure 6).

9 patients were HIV reactive (16.4%),4 were HCV reactive (7.3%).2 patients had both HIV and HCV infection (table 11). 1 out of these 2 had tubercular meningitis and the other 1 had cryptococcal meningitis.4 patients with HIV infection had cryptococcal meningitis,2 patients with

HIV had tubercular meningitis and 1 had viral meningitis (table 12,figure7).

6 patients were diabetic.5 patients of subacute meningitis (10.9%) had diabetes and 1 patient of chronic meningitis (11.1%) had diabetes.2 patients of chronic meningitis (22.2%) had h/o tuberculosis(table 13). 1 of these had cryptococcal meningitis,4 out of these had tubercular meningitis and 1 had viral meningitis. 2 had h/o tuberculosis (3.6%). Both of them later had tubercular meningitis (table 14).

Mean GCS was 13 in both subacute and chronic meningitis. Mean pulse rate was 88/min., mean SBP was 117.67mmHg, mean DBP was 72.25mmHg and mean temperature was 98.99 F (table 15). Mean GCS was 12.78 in tubercular meningitis and it was 14.50 in both viral and cryptococcal meningitis. Mean pulse rate was 88.56 in tubercular meningitis and it was 85.50 and 93.50 in cryptococcal and viral meningitis respectively. Mean SBP was 120.09 in tubercular meningitis,110 in cryptococcal meningitis and viral meningitis. Mean DBP was 73.11 in tubercular,70 in both viral and cryptococcal meningitis. Mean temperature was 99.36 in tubercular meningitis,99.08 in cryptococcal meningitis,99.50 in viral meningitis (table 16, figure 8).

Mean TLC seen on admission was 10.34 x 10^3/mm^3 and 12.51 x 10^3/mm^3 in subacute and chronic meningitis respectively. Mean ESR on admission was 45.25 and 44.86 in subacute and chronic meningitis respectively. Mean Total bilirubin was 0.77mg/dl and 0.69mg/dl on admission in subacute and chronic meningitis respectively. Mean SGOT on admission were 44.24U/L and 62U/L in subacute and chronic meningitis respectively and mean SGPT was 50.89U/L and 71.33U/L in subacute and chronic meningitis respectively (table 17). Mean TLC seen on admission was 11.24, 8.88, 7.20 (x 10^3/mm^3) in tubercular, cryptococcal and viral meningitis respectively. Mean ESR was 46.18, 35.80, 49.50(mm/hr) in tubercular, cryptococcal and viral meningitis respectively. Mean total bilirubin on admission was 0.66, 1.37,

0.81(mg/dl) in tubercular, cryptococcal and viral meningitis respectively. Mean SGOT was 45.69,64.33 and 35.67 (U/L) and mean SGPT on admission was 55.36, 61.50 and 24.00(U/L) in tubercular, cryptococcal and viral meningitis respectively (table 18,figure 9).

Mean protein in CSF was found to be 123.50 and 131.14(mg/dl) and mean glucose was found to be 47.12 and 41.67(mg/dl) in subacute and chronic meningitis respectively. Mean TLC was found to be 75.08 and 105.11(x $10^3/mm^3$) in subacute and chronic meningitis respectively with lymphocytic predominance in 50 patients. Mean ADA was found to be 15.80 and 41.75(U/L) in subacute and chronic meningitis respectively (table 19). Mean protein in CSF was 121.20, 153.28, 121.93(mg/dl) in tubercular, cryptococcal, viral meningitis respectively. Mean glucose was 44.78, 50.73, 55.75 (mg/dl) in tubercular, cryptococcal, viral meningitis respectively. Mean TLC was 87.84, 62.33 and 18.13(x $10^3/mm^3$) in tubercular, cryptococcal, viral meningitis respectively. ADA was more than 10 in 42 patients and less than 10 in 12 patients. Mean ADA was 22, 12.16 and 11.42(U/L) in tubercular, cryptococcal, viral meningitis respectively (table 20, figure 10).

CBNAAT was positive in 19 cases of subacute meningitis (41.3%) and in 3 cases of chronic meningitis (33.3%). Cryptococcal antigen was positive in 5 cases of subacute meningitis (10.9%) and 1 case of chronic meningitis (11.1%). HSV was positive in 2 cases of subacute meningitis (4.3%) (table 21). CBNAAT was positive in 22 patients of tubercular meningitis. Cryptococcal antigen was positive in 5 patients of subacute meningitis (10.9%) and 1 patient of chronic meningitis (11.1%). HSV was positive in 2 cases of viral meningitis (50%) (table 22, figure 11).

Papilledema was seen in 8 patients (17.4%) of subacute meningitis and 1 patient of chronic meningitis (11.1%) while choroid tubercles were seen in 2 patients of subacute meningitis (4.3%) (table 23). Papilledema was seen in 7 cases of tubercular meningitis (15.6%),2 cases of cryptococcal meningitis (33.3%) and none of the cases of viral meningitis. Choroid

tubercles were seen in 2 cases of tubercular meningitis (4.4%) (table 24, figure 12)

The most common abnormal brain MRI findings were leptomeningeal enhancement (32.7%), hydrocephalus (18.2%), granulomas (7.3%), vasculitic infarcts (3.6%). The most common MRI finding in subacute meningitis was meningeal enhancement seen in 11 patients (23.9%).In case of chronic meningitis, only 2 patients had positive MRI findings. One had meningeal enhancement only and the other one had hydrocephalus and meningeal enhancement. Among patients of subacute meningitis, 3 patients had hydrocephalus and meningeal enhancement (6.5%), 1 had hydrocephalus and granulomas (2.2%), 1 patient had meningeal enhancement and granulomas (2.2%) ,1 had meningeal enhancement and vasculitic infarcts (2.2%),1 had vasculitic infarcts and granulomas (2.2%) (table 25, figure 13). Hydrocephalus was seen in 2 patients of cryptococcal meningitis (33.3%). The most common MRI finding in tubercular meningitis was meningeal enhancement (40%) followed by hydrocephalus (17.8%), followed by granulomas (8.9%) and vasculitic infarcts (4.4%). None of the findings were seen on MRI of patients with viral meningitis (table 26, figure 14).

The mean length of stay in ward was 6.15 days and 7.33 days in subacute and chronic meningitis respectively and in ICU was 4.60days (table 27). The mean length of stay in ward was 5.57 days for tubercular meningitis,8 days for cryptococcal meningitis,12.50 days for viral meningitis. The mean length of stay in ICU was 4.86 days for tubercular meningitis,2 days for cryptococcal meningitis,5 days for viral meningitis (table 28).

Out of 55 admitted patients,37 patients got discharged;30 were cases of subacute meningitis(65.2%) and 7 were chronic meningitis(77.8%).10 were discharged on request; 9 were subacute meningitis(19.6%)and 1 was chronic meningitis(11.1%).8 patients were discharged against medical advice.7 were subacute meningitis(15.2%) and 1 was chronic meningitis (11.1%)(table 29).5 patients of cryptococcal meningitis got

discharged (83.3%), 1 got discharged against medical advice (16.7%). 29 patients of tubercular meningitis were discharged (64.4%), 10 were discharged on request (22.2%), 6 were discharged against medical advice (13.3%).3 patients of viral meningitis were discharged (75%), 1 was discharged on request (25%) (table 30, figure 15).

On 2 months follow up, 41 patients improved clinically(74.5%) with complete resolution of symptoms and signs, 34 patients were subacute and 7 were chronic. 4 improved partially (7.3%) with one or more residual symptoms or signs persisting at time of follow up; 3 were subacute and 1 was chronic.7 patients were lost to follow up (16.4%),1 patient worsened (1.8%), 2 got expired. Those 2 patients who got expired had been discharged against medical advice and no further hospitalization was continued by them (table 31). Out of 6 cases of cryptococcal meningitis, 4 improved clinically (66.7%) and 1 got expired and one was lost to follow up at 2 months (%). Out of 45 cases of tubercular meningitis, 34 cases improved clinically (75.6%), 4 improved partially (8.9%), 5 were lost to follow up (%),1 patient worsened (2.2%) due to non-compliance to treatment and 1 got expired. Out of 4 cases of viral meningitis, 3 patients improved clinically (75%), 1 was lost to follow up (25%) (table 32,figure 16).

On 4 months follow up, out of 46 cases, 39 patients improved clinically (84.8%), 2 improved partially (4.3%), 5 were lost to follow up (10.9%), 32 patients of subacute meningitis improved clinically and 7 patients of chronic meningitis improved clinically. 2 patients of subacute meningitis improved partially (table 33). Out of 4 patients of cryptococcal meningitis on 4 months follow up, all of them improved clinically (100%). Out of 39 patients of tubercular meningitis, 32 patients improved clinically (82.1%), 2 improved partially (5.1%). 5 patients were lost to follow up (12.8%), Out of 3 cases of viral meningitis, all of them improved clinically on 4 months follow up (table 34, figure 17).

Table 3: Distribution according to duration of illness

Duration of illness	No. of cases	Percentage
5- 30days	46	83.6%
>30 days	9	16.4%

Figure 1: Distribution according to duration of illness

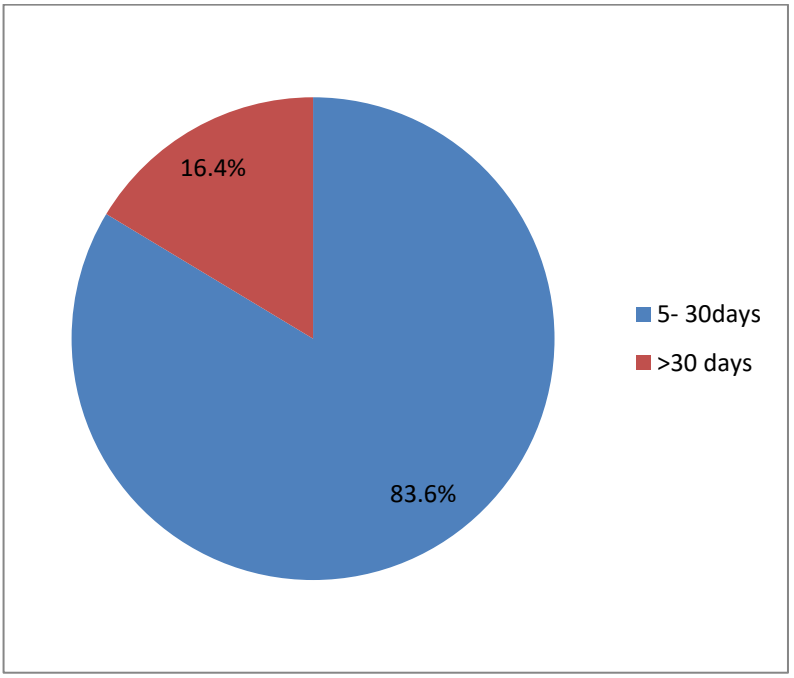


Table 4: Distribution according to outcome diagnosis

		Outcome Diagnosis						Total	Chi-square value	p-value
		Cryptococcal meningitis	Cryptococcal meningitis	Tubercular meningitis	Tubercular meningitis	Viral meningitis	Viral meningitis			
Duration of Illness	> 30 DAYS	1	16.7%	8	17.8%	0	0.0%	9	0.849	0.654
	5-30 DAYS	5	83.3%	37	82.2%	4	100.0%	46		
Total		6	100.0%	45	100.0%	4	100.0%	55		

Figure 2: Distribution according to outcome diagnosis

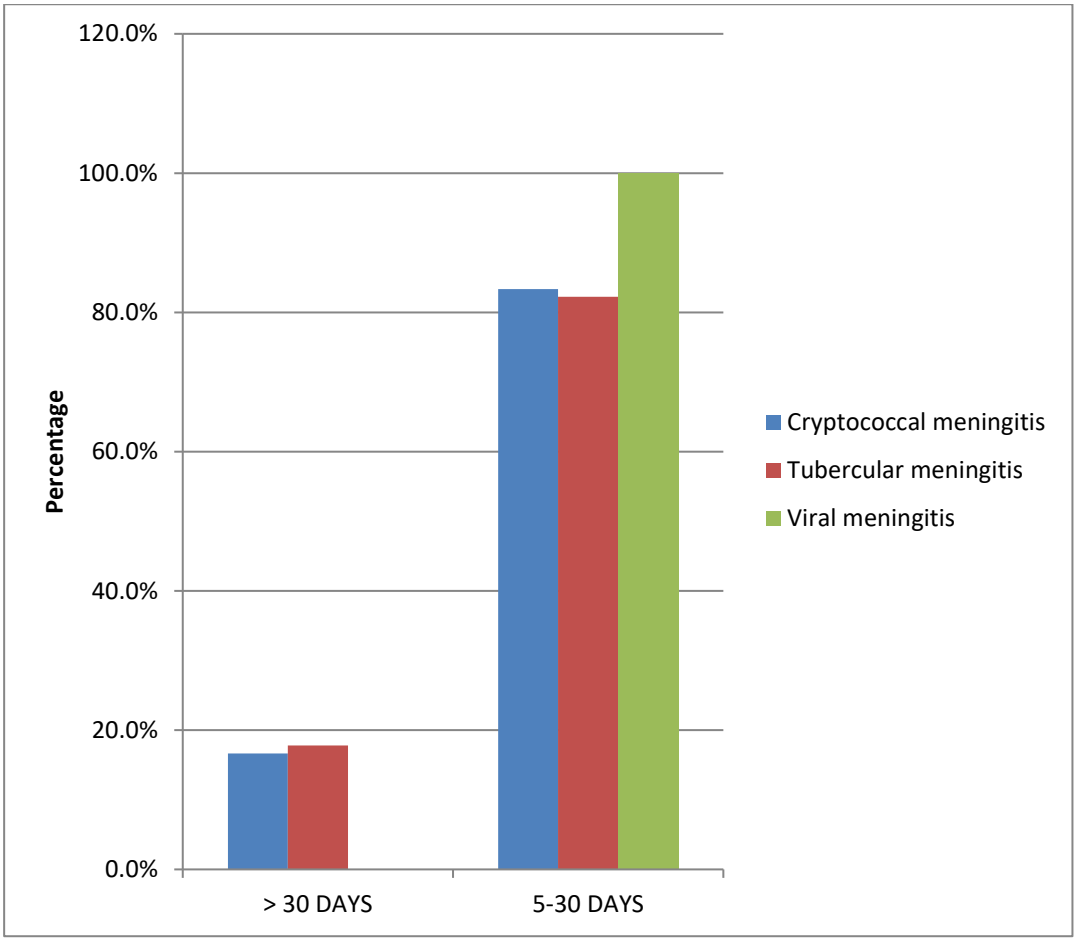


Table 5: Distribution according to age and gender

		Subacute (n=46)		Chronic (n=9)		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age			
Age group	< 30	9	19.6%	5	55.6%	14	7.213	0.125
	31-40	11	23.9%	1	11.1%	12		
	41-50	10	21.7%	0	0.0%	10		
	51-60	6	13.0%	2	22.2%	8		
	> 60	10	21.7%	1	11.1%	11		
Gender	F	23	50.0%	1	11.1%	24	4.629	0.062
	M	23	50.0%	8	88.9%	31		

Table 6: Distribution according to outcome diagnosis and age & gender

		Outcome Diagnosis						Total	Chi-square value	p-value
		Cryptococcal meningitis		Tubercular meningitis		Viral meningitis				
Age group	< 30	2	33.3%	12	26.7%	0	0.0%	14	9.861	0.275
	31-40	3	50.0%	8	17.8%	1	25.0%	12		
	41-50	0	0.0%	8	17.8%	2	50.0%	10		
	51-60	1	16.7%	6	13.3%	1	25.0%	8		
	> 60	0	0.0%	11	24.4%	0	0.0%	11		
Gender	F	0	0.0%	21	46.7%	3	75.0%	24	6.413	0.040
	M	6	100.0%	24	53.3%	1	25.0%	31		

Figure 3: Distribution according to outcome diagnosis and age

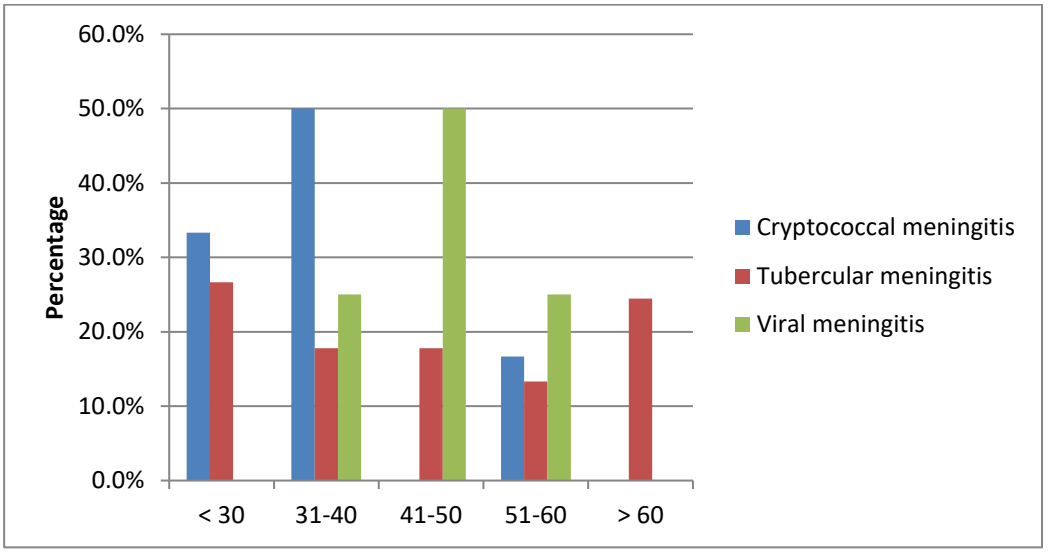


Figure 4: Distribution according to outcome diagnosis and gender

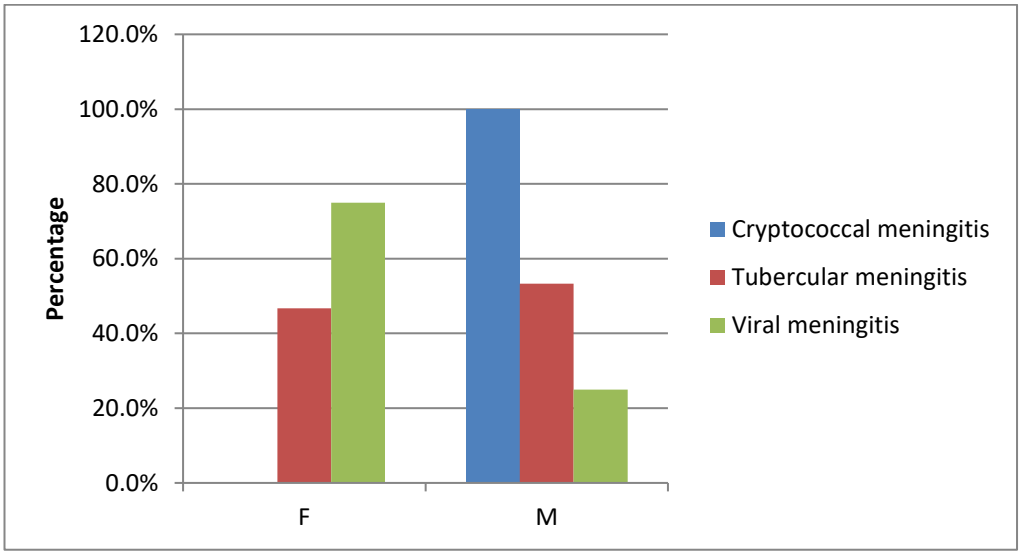


Table 7-Distribution according to symptoms

		Subacute (n=46)		Chronic (n=9)		Total	Chi-square value	p-value
Symptoms		No. of cases	%age	No. of cases	%age			
Altered sensorium	Yes	36	78.3%	5	55.6%	41	2.045	0.153
Fever	Yes	31	67.4%	7	77.8%	38	0.380	0.705
Headache	Yes	16	34.8%	5	55.6%	21	1.376	0.279
Seizure	Yes	10	21.7%	2	22.2%	12	0.001	0.974
Vomiting	Yes	19	41.3%	3	33.3%	22	0.199	0.655

Figure 5: Distribution according to outcome diagnosis and symptoms

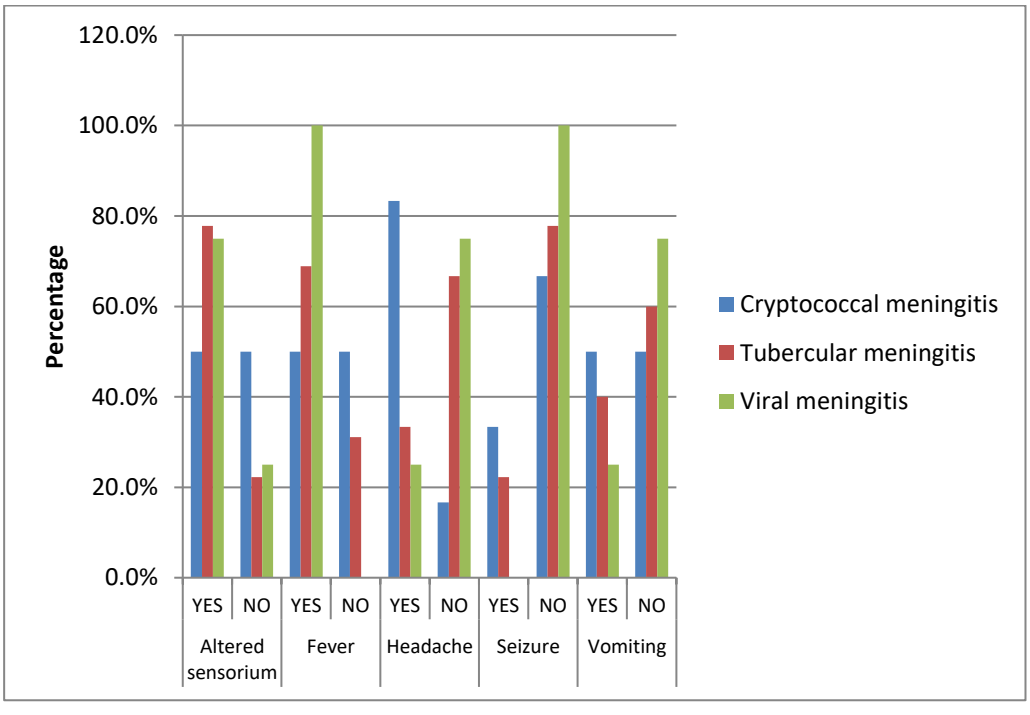


Table 8: Distribution according to outcome diagnosis and symptoms

		Outcome Diagnosis						Total	Chi-square value	p-value
Symptoms		Cryptococcal meningitis	Cryptococcal meningitis	Tubercular meningitis	Tubercular meningitis	Viral meningitis	Viral meningitis			
Altered sensorium	Yes	3	50.0%	35	77.8%	3	75.0%	41	2.153	0.341
	No	3	50.0%	10	22.2%	1	25.0%	14		
Fever	Yes	3	50.0%	31	68.9%	4	100.0%	38	2.814	0.245
	No	3	50.0%	14	31.1%	0	0.0%	17		
Headache	Yes	5	83.3%	15	33.3%	1	25.0%	21	5.925	0.052
	No	1	16.7%	30	66.7%	3	75.0%	34		
Seizure	Yes	2	33.3%	10	22.2%	0	0.0%	12	1.587	0.452
	No	4	66.7%	35	77.8%	4	100.0%	43		
Vomiting	Yes	3	50.0%	18	40.0%	1	25.0%	22	0.625	0.732
	No	3	50.0%	27	60.0%	3	75.0%	33		
Total		6	100.0%	45	100.0%	4	100.0%	55		

Table 9: Distribution according to signs

		Subacute (n=46)		Chronic (n=9)		Total	Chi-square value	p-value
Signs		No. of cases	%age	No. of cases	%age			
Neck rigidity	Yes	35	76.1%	3	33.3%	38	6.443	0.019
Cranial nerve palsy	Lt 6th nerve palsy	0	0.0%	1	11.1%	1	7.360	0.118
	Rt 3rd nerve,Lt 6th nerve palsy	1	2.2%	0	0.0%	1		
	Rt 6th nerve palsy	1	2.2%	1	11.1%	2		
	Rt 7th nerve palsy	1	2.2%	0	0.0%	1		

Table 10: Distribution according to outcome diagnosis and signs

		Outcome Diagnosis						Total	Chi-square value	p-value
		Cryptococcal meningitis (n=6)		Tubercular meningitis (n=45)		Viral meningitis (n=4)				
Neck rigidity	Yes	3	50.0%	33	73.3%	2	50.0%	38	2.086	0.352
Cranial nerve palsy	Left 6th nerve palsy	0	0.0%	1	2.2%	0	0.0%	1	3.936	0.863
	Rt 3rd nerve and Lt 6th nerve palsy	0	0.0%	1	2.2%	0	0.0%	1		
	Rt 6th nerve palsy	1	16.7%	1	2.2%	0	0.0%	2		
	Rt 7th nerve palsy	0	0.0%	1	2.2%	0	0.0%	1		

Figure 6: Distribution according to Cranial nerve palsy

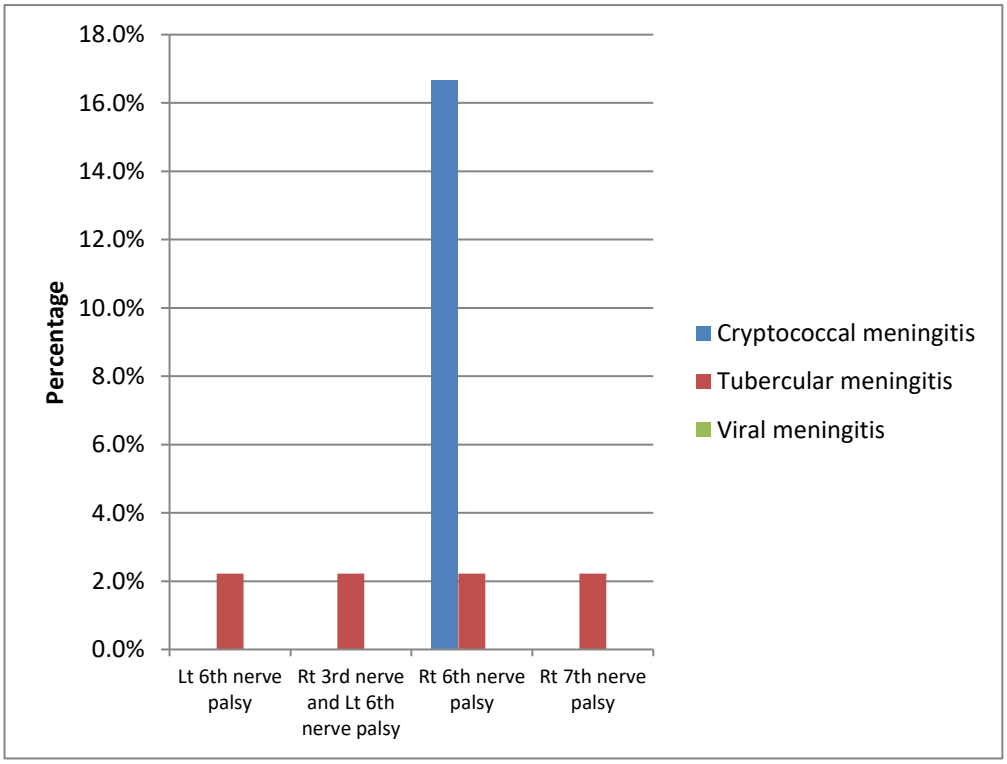


Table 11: Distribution according to viral markers

		Subacute (n=46)		Chronic (n=9)		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age			
Viral markers (HIV/HCV/HBSAg)	HCV	2	4.3%	0	0.0%	2	1.552	0.670
	HIV	5	10.9%	2	22.2%	7		
	HIV, HCV	2	4.3%	0	0.0%	2		
	NR	37	80.4%	7	77.8%	44		
Total		46	100.0%	9	100.0%	55		

Table 12: Distribution according to outcome diagnosis and viral markers

		Outcome Diagnosis						Total	Chi-square value	p-value
		Cryptococcal meningitis	Cryptococcal meningitis	Tubercular meningitis	Tubercular meningitis	Viral meningitis	Viral meningitis			
Viral Markers (HIV/HCV/HBSAg)	HCV	0	0.0%	2	4.4%	0	0.0%	2	23.719	0.001
	HIV	4	66.7%	2	4.4%	1	25.0%	7		
	HIV, HCV	1	16.7%	1	2.2%	0	0.0%	2		
	NR	1	16.7%	40	88.9%	3	75.0%	44		
Total		6	100.0%	45	100.0%	4	100.0%	55		

Figure 7: Distribution according to outcome diagnosis and viral markers

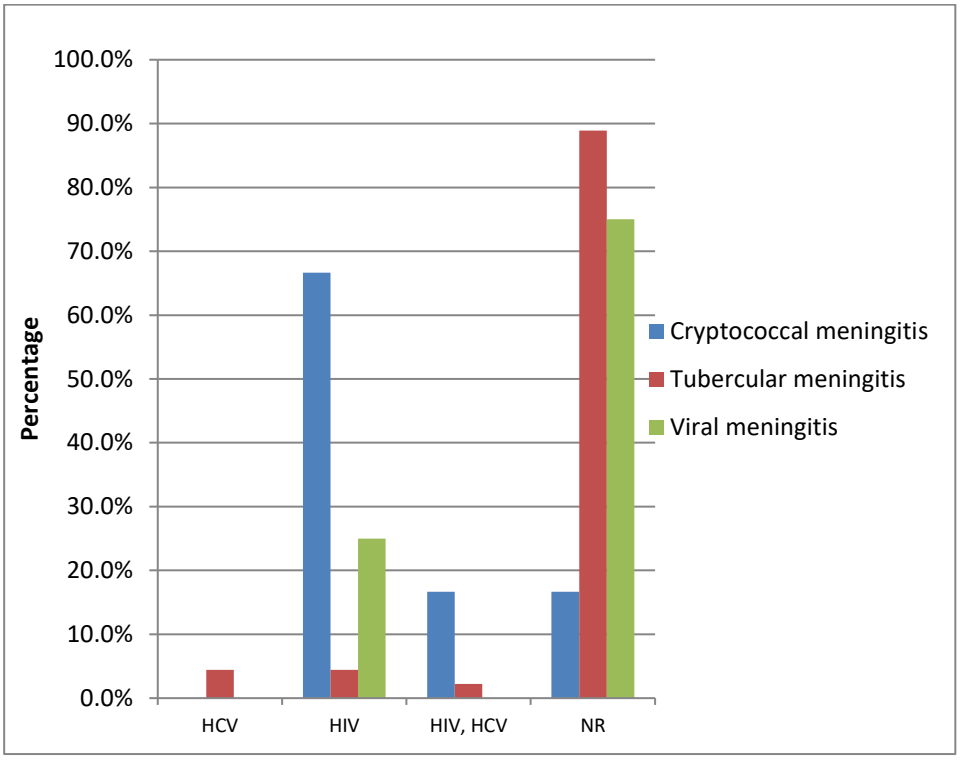


Table 13: Distribution according to past history

		Subacute (n=46)		Chronic (n=9)		Total	Chi-square value	p-value
Past history		No. of cases	%age	No. of cases	%age			
Diabetes mellitus	Yes	5	10.9%	1	11.1%	6	0.000	1.000
Tuberculosis	Yes	0	0.0%	2	22.2%	2	10.608	0.024
Seizure disorder	Yes	0	0.0%	0	0.0%	0		

Table 14: Distribution according to outcome diagnosis and past history

		Outcome Diagnosis						Total	Chi-square value	p-value
Past History		Cryptococcal meningitis	Cryptococcal meningitis	Tubercular meningitis	Tubercular meningitis	Viral meningitis	Viral meningitis			
Diabetes Mellitus	Yes	1	16.7%	4	8.9%	1	25.0%	6	1.211	0.546
	No	5	83.3%	41	91.1%	3	75.0%	49		
Tuberculosis	Yes	0	0.0%	2	4.4%	0	0.0%	2	0.461	0.794
	No	5	83.3%	43	95.6%	4	100.0%	52		
Seizure Disorder	Yes	0	0.0%	0	0.0%	0	0.0%	O		
	No	6	100.0%	45	100.0%	4	100.0%	55		
Total		6	100.0%	45	100.0%	4	100.0%	55		

Table 15: Distribution according to vitals

	Subacute (n=46)		Chronic (n=9)		Z	p-value
Vitals	Mean	SD	Mean	SD		
GCS	13.09	2.62	13.11	2.62	0.025	0.980
Pulse(/Min.)	87.76	11.71	92.78	12.33	1.166	0.249
SBP(mmHg)	119.65	11.25	111.11	10.54	-2.103	0.040
DBP(mmHg)	73.04	6.28	70.00	10.00	-1.198	0.236
Temperature(F)	99.33	0.49	99.40	0.32	0.435	0.665

Table 16: Distribution according to outcome diagnosis and vitals

Vitals	Cryptococcal meningitis	Tubercular meningitis	Viral meningitis
	Mean	Mean	Mean
GCS	12.78	14.50	14.50
Pulse(/min.)	88.56	85.50	93.50
SBP(mmHg)	120.09	110.00	110.00
DBP(mmHg)	73.11	70.00	70.00
Temperature(F)	99.36	99.08	99.50

Figure 8: Distribution according to outcome diagnosis and vitals

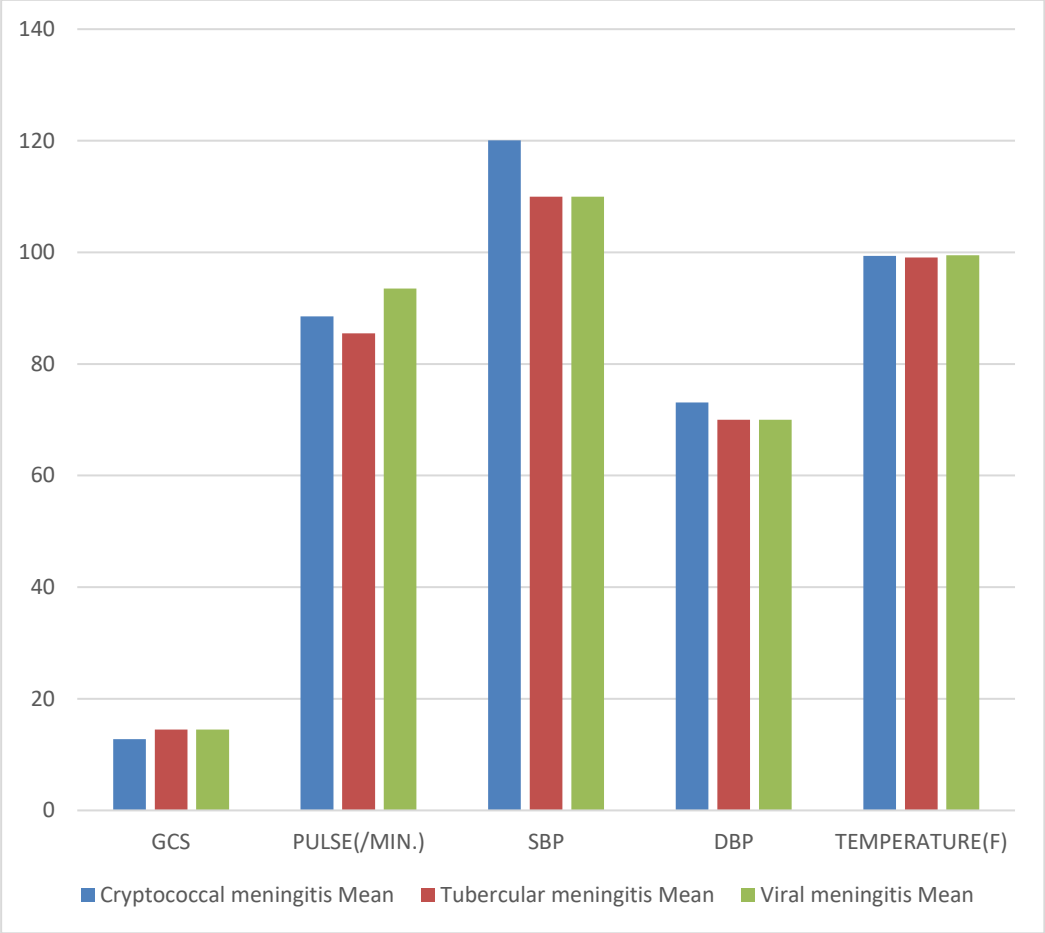


Table 17: Distribution according to blood investigations

	Subacute (n=46)		chronic (n=9)		Z	p-value
Investigations	Mean	SD	Mean	SD		
TLC(Adm) X10^3	10.34	4.22	12.51	4.57	1.398	0.168
TLC(Dis) X10^3	11.36	4.48	10.07	5.90	-0.693	0.492
ESR(Adm)	45.25	21.15	44.86	20.63	-0.050	0.960
Total Bil(Adm)	0.77	0.81	0.69	0.25	-0.291	0.772
Total Bil (Dis)	0.62	0.27	0.62	0.49	0.006	0.996
SGOT(Adm)	44.24	24.88	62.00	32.88	1.851	0.070
SGOT(Dis)	75.59	154.89	50.00	35.83	-0.430	0.669
SGPT(Adm)	50.89	51.25	71.33	40.41	1.126	0.265
SGPT(Dis)	95.19	150.65	52.57	33.97	-0.737	0.466

Table 18: Distribution according to outcome diagnosis and blood investigations

Investigations	Cryptococcal meningitis	Tubercular meningitis	Viral meningitis
	Mean	Mean	Mean
TLC(Adm) X10^3	11.24	8.88	7.20
TLC(Dis) X10^3	11.56	10.40	7.23
ESR(Adm)	46.18	35.80	49.50
Total Bil (Adm)	0.66	1.37	0.81
Total Bil (Dis)	0.64	0.75	0.41
SGOT(Adm)	45.69	64.33	35.67
SGOT(Dis)	51.12	471.50	29.33
SGPT(Adm)	55.36	61.50	24.00
SGPT(Dis)	76.18	372.00	26.67

Figure 9: Distribution according to outcome diagnosis and blood investigations

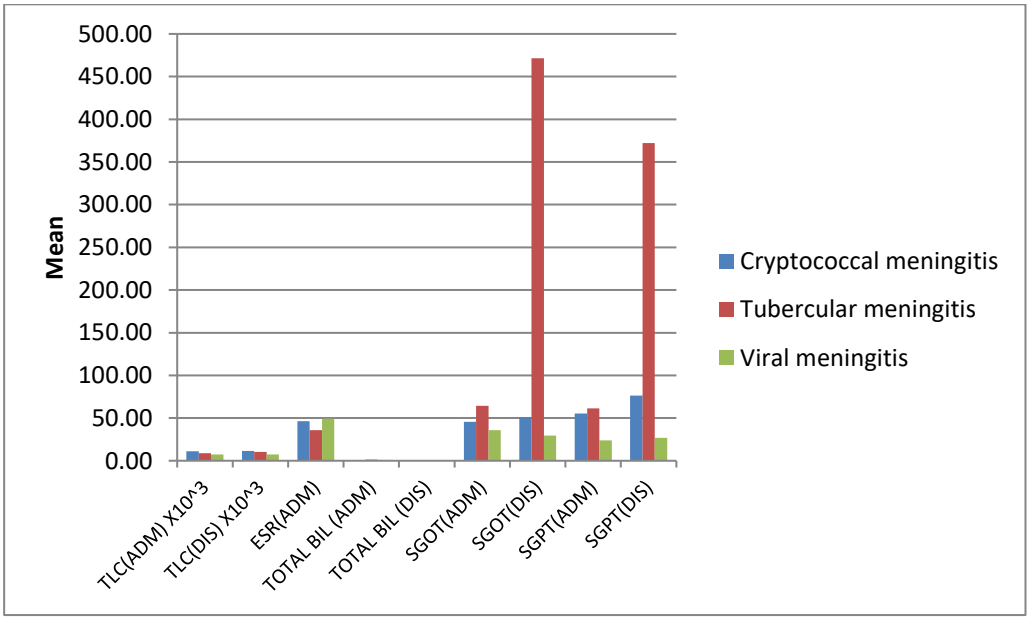


Table 19: Distribution according to CSF findings

CSF findings	Subacute (n=46)		chronic (n=9)		Z	p-value
	Mean	SD	Mean	SD		
Protein	123.50	77.43	131.14	122.62	0.245	0.808
Glucose	47.12	27.07	41.67	22.44	-0.566	0.574
Chloride	113.24	17.16	118.56	7.54	0.906	0.369
TLC	75.08	99.55	105.11	123.67	0.796	0.430
MNC	86.91	18.30	77.78	32.7	-1.187	0.241
Neutrophils	13.09	18.30	22.22	32.7	1.187	0.241
ADA	15.80	9.67	41.75	50.35	3.280	0.002

Table 20: Distribution according to outcome diagnosis and CSF findings

CSF findings	Cryptococcal meningitis	Tubercular meningitis	Viral meningitis
	Mean	Mean	Mean
Protein	121.20	153.28	121.93
Glucose	44.78	50.73	55.75
Chloride	113.29	118.20	118.50
TLC	87.84	62.33	18.13
MNC	86.78	73.83	87.50
Neutrophils	13.22	26.17	12.50
ADA	22	12.16	11.42

Figure 10: Distribution according to outcome diagnosis and CSF findings

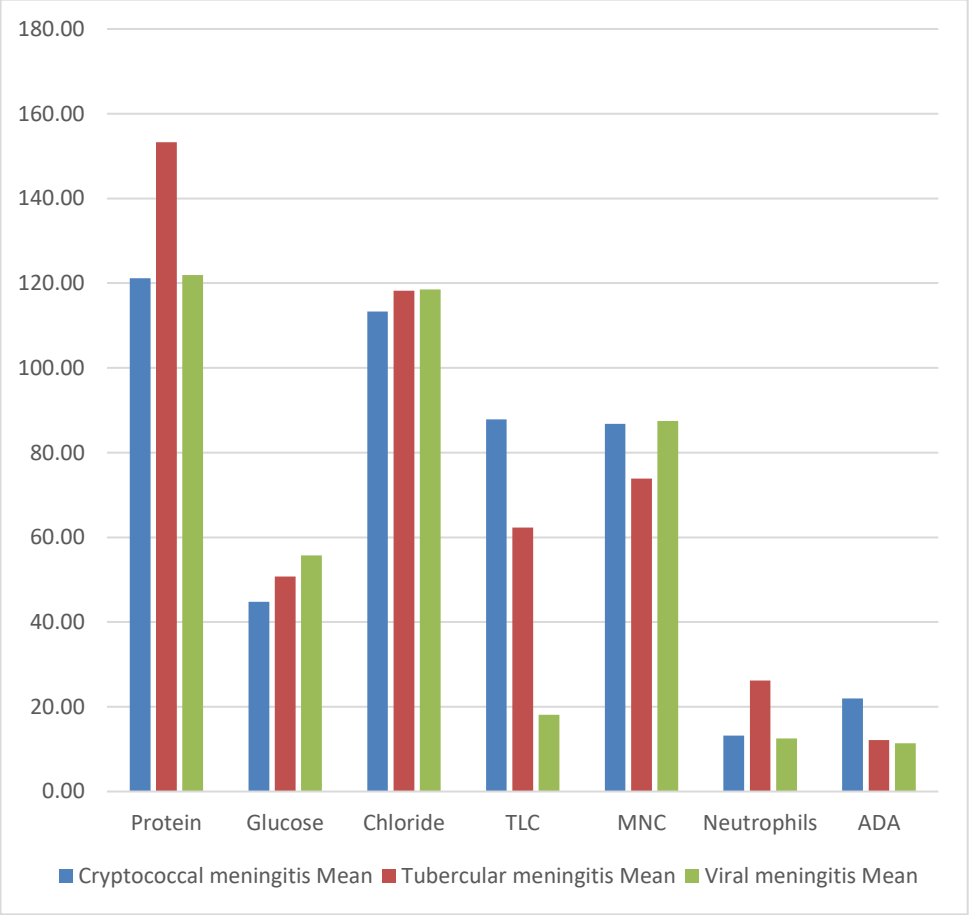


Table 21: Distribution according to CSF microbiology

		Subacute (n=46)		Chronic (n=9)		Total	Chi-square value	p-value
CSF Microbiology		No. of cases	%age	No. of cases	%age			
CBNAAT	Positive	19	41.3%	3	33.3%	22	0.199	0.655
	Negative	27	58.7%	6	66.7%	33		
Cryptococcal	Positive	5	10.9%	1	11.1%	6	0.000	1.000
	Negative	41	89.1%	8	88.9%	49		
HSV	Positive	2	4.3%	0	0.0%	2	0.406	0.524
	Negative	44	95.7%	9	100.0%	53		

Table 22: Distribution according to outcome diagnosis and CSF microbiology

		Outcome diagnosis						Total	Chi-square value	p-value
CSF Microbiology		Cryptococcal meningitis		Tubercular meningitis		Viral meningitis				
CBNAAT	Positive	0	0.0%	22	48.9%	0	0.0%	22	8.148	0.017
	Negative	6	100.0%	23	51.1%	4	100.0%	33		
Cryptococcal	Positive	6	100.0%	0	0.0%	0	0.0%	6	55.000	0.001
	Negative	0	0.0%	45	100.0%	4	100.0%	49		
HSV	Positive	0	0.0%	0	0.0%	2	50.0%	2	26.462	0.001
	Negative	6	100.0%	45	100.%	2	50.0%			

Figure 11: Distribution according to outcome diagnosis and CSF microbiology

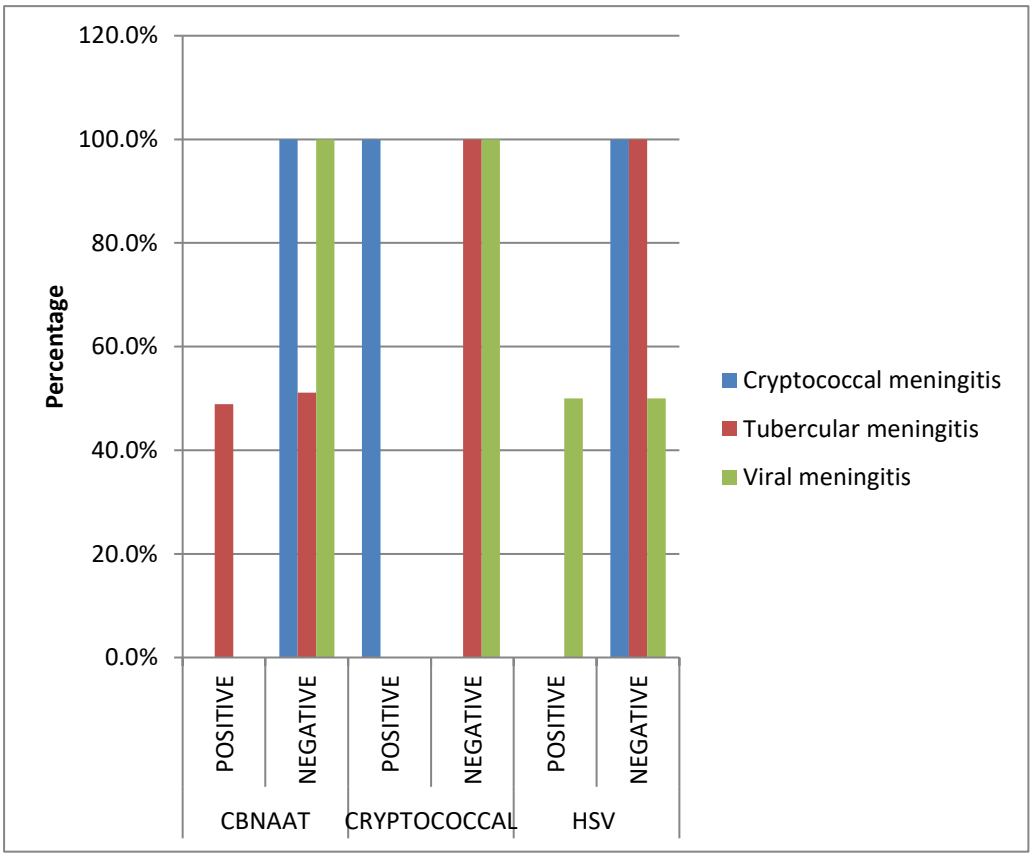


Table 23: Distribution according to fundus examination

		Subacute (n=46)		Chronic (n=9)		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age			
Fundus	Choroid tubercles	2	4.3%	0	0.00%	2	0.679	0.712
	Papilledema	8	17.4%	1	11.10%	9		

Table 24: Distribution according to outcome diagnosis and fundus examination

		Outcome Diagnosis						Total	Chi-square value	p-value
		Cryptococcal meningitis	Cryptococcal meningitis	Tubercular meningitis	Tubercular meningitis	Viral meningitis	Viral meningitis			
	Choroid Tubercles	0	0.0%	2	4.4%	0	0.0%	2	2.506	0.644
	Papiiledema	2	33.3%	7	15.6%	0	0.0%	9		
Total		6	100.0%	45	100.0%	4	100.0%	55		

Figure 12: Distribution according to outcome diagnosis and fundus examination

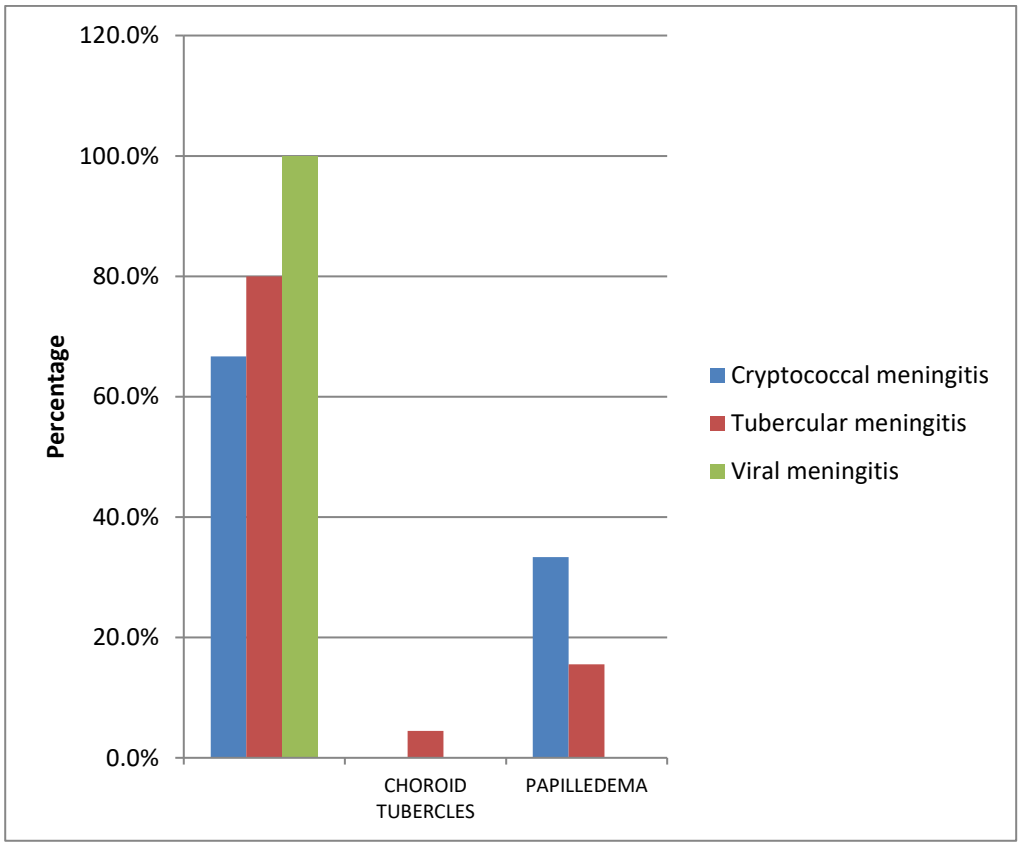


Table 25: Distribution according to MRI findings

						Total	Chi-square value	p-value
		No. of cases	Subacute (n=46)	No. of cases	Chronic (n=9)			
MRI Findings	Meningeal enhancement only	11	23.9%	1	11.1%	12		
	Meningeal enhancement and hydrocephalus	3	6.5%	1	11.1%	4		
	Meningeal enhancement and granulomas	1	2.2%	0	0.0%	1		
	Meningeal enhancement and vasculitic infarcts	1	2.2%	0	0.0%	1	4.630	0.865
	Hydrocephalus only	5	10.9%	0	0.0%	5		
	Hydrocephalus and granulomas	1	2.2%	0	0.0%	1		
	Granulomas	1	2.2%	0	0.0%	1		
	Vasculitic infarcts and granulomas	1	2.2%	0	0.0%	1		

Figure 13: Distribution according to MRI findings

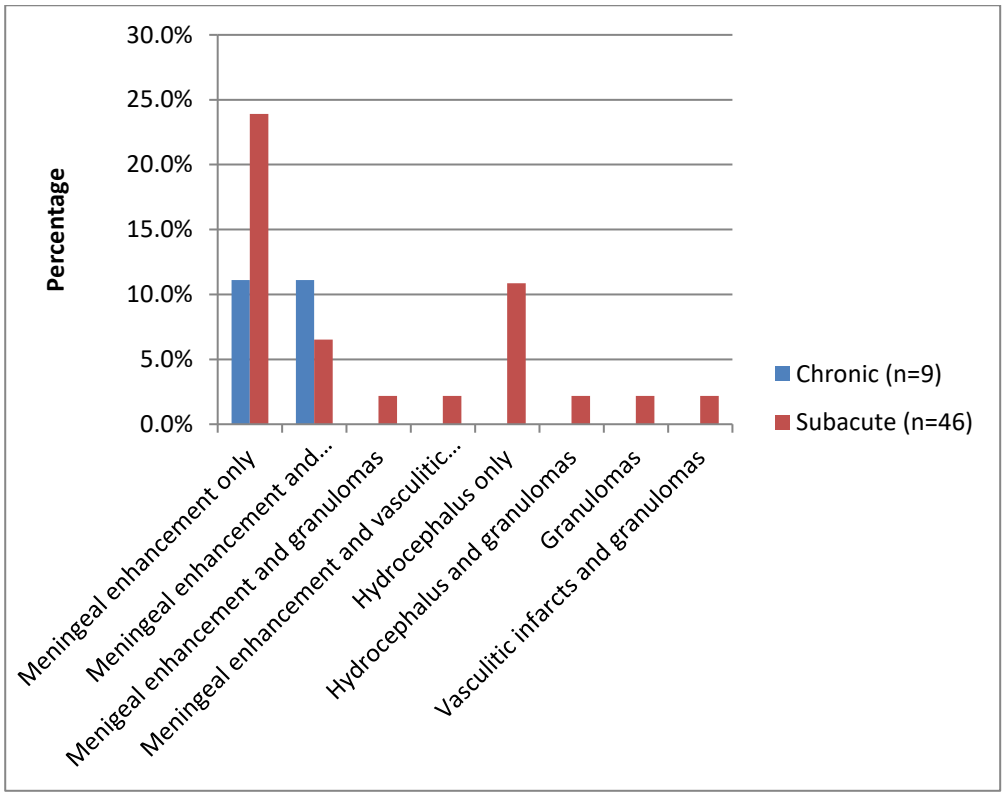


Table 26: Distribution according to outcome diagnosis and MRI findings

		Outcome Diagnosis						Total	Chi-square value	p-value
		Cryptococcal meningitis	Cryptococcal meningitis	Tubercular meningitis	Tubercular meningitis	Viral meningitis	Viral meningitis			
Meningeal enhancement	Yes	0	0.0%	18	40.0%	0	0.0%	18	5.946	0.051
	No	6	100.0%	27	60.0%	4	100.0%	37		
Hydrocephalus	Yes	2	33.3%	8	17.8%	0	0.0%	10	1.820	0.403
	No	4	66.7%	37	82.2%	4	100.0%	45		
Vasculitic infarcts	Yes	0	0.0%	2	4.4%	0	0.0%	2	0.461	0.794
	No	6	100.0%	43	95.6%	4	100.0%	53		
Granulomas	Yes	0	0.0%	4	8.9%	0	0.0%	4	0.959	0.619
	No	6	100.0%	41	91.1%	4	100.0%	51		
Total		6	100.0%	45	100.0%	4	100.0%	55		

Figure 14: Distribution according to outcome diagnosis and MRI findings

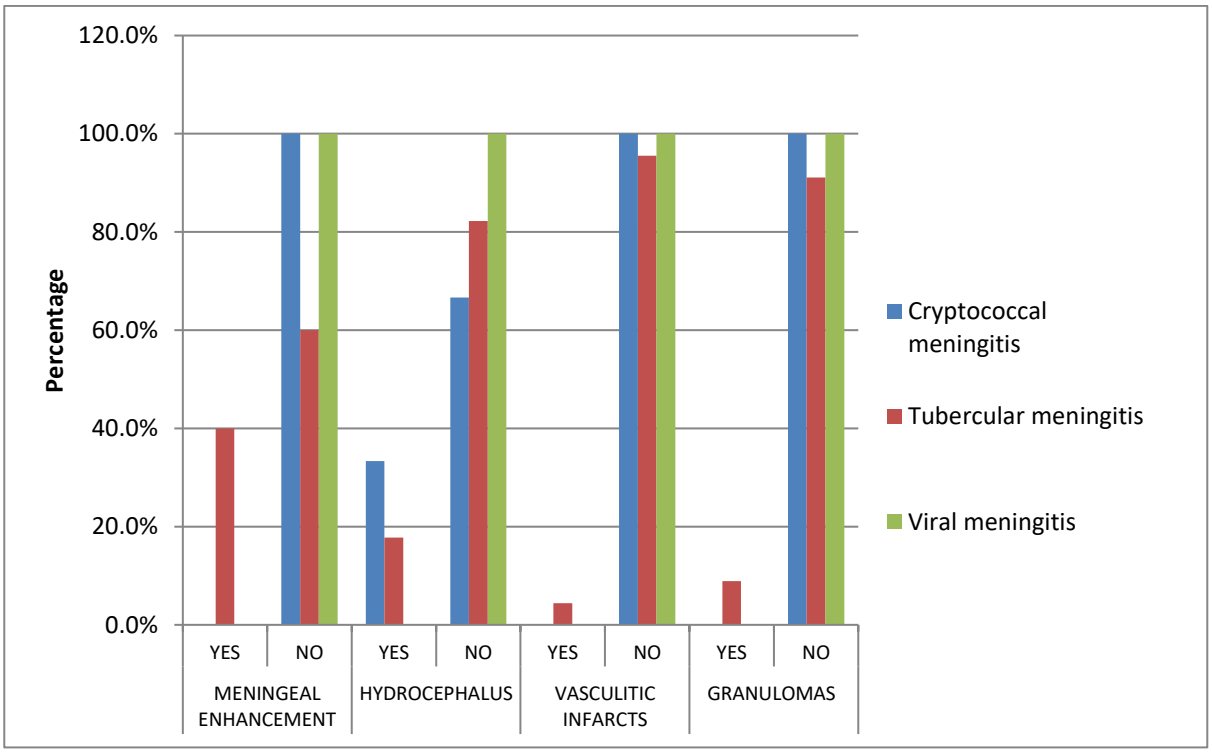


Table 27: Distribution according to length of stay

	Subacute (n=46)		Chronic (n=9)		Z	p-value
	Mean	SD	Mean	SD		
Length of stay in ward (In days)	6.15	4.56	7.33	4.92	0.702	0.486
Length of stay in ICU (In days)	4.59	5.52	4.33	7.73	-0.118	0.907

Table 28: Distribution according to outcome diagnosis and length of stay

	Cryptococcal meningitis	Tubercular meningitis	Viral meningitis
	Mean	Mean	Mean
Length of stay in ward (in days)	5.57	8.00	12.50
Length of stay in ICU (in days)	4.86	2.00	5.00

Table 29: Distribution according to outcome

Outcome		No. of cases	Subacute (n=46)	No. of cases	Chronic (n=9)	Total	Chi-square value	p-value
Discharge	Yes	30	65.2%	7	77.8%	37	0.539	0.463
DAMA	Yes	7	15.2%	1	11.1%	8	0.102	0.749
DOR	Yes	9	19.6%	1	11.1%	10	0.362	0.548

Table 30: Distribution according to outcome and outcome diagnosis

	Outcome Diagnosis						Total	Chi-square value	p-value
Outcome	Cryptococcal meningitis	Cryptococcal meningitis	Tubercular meningitis	Tubercular meningitis	Viral meningitis	Viral meningitis			
Discharge	5	83.3%	29	64.4%	3	75.0%	37	2.906	0.574
DAMA	1	16.7%	6	13.3%	1	25.0%	8		
DOR	0	0.0%	10	22.2%	0	0.0%	10		
Total	6	100.0%	45	100.0%	4	100.0%	55		

Figure 15: Distribution according to outcome and outcome diagnosis

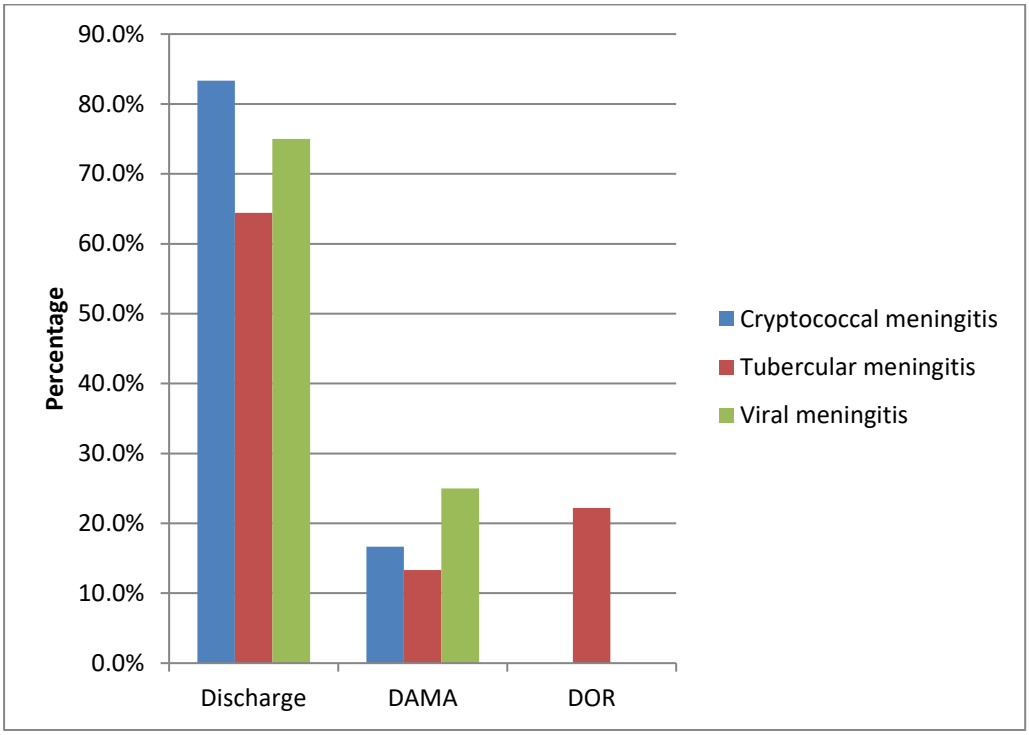


Table 31: Distribution according to outcome at 2 months follow up

						Total	Chi-square value	p-value
		No. of cases	Subacute (n=46)	No. of cases	Chronic (n=9)			
	Improved clinically	34	73.90%	7	77.80%	41		
	Improved partially	3	6.50%	1	11.10%	4		
2 Months (Improved clinically/Improved Partially/Worsened/Death)	Loss to Follow up	6	13.0%	1	11.1%	7	0.610	0.894
	Death	2	4.3%	0	0.0%	2		
	Worsened	1	2.2%	0	0.0%	1		
Total		46	100.0%	9	100.0%	55		

Table 32: Distribution according to outcome diagnosis and outcome at 2 months follow up

		Outcome Diagnosis						Total	Chi-square value	p-value
		Cryptococcal meningitis		Tubercular meningitis		Viral meningitis				
	Improved clinically	4	66.7%	34	75.6%	3	75.0%	41		
2 Months (Improved clinically/Improved Partially/Worsened)	Loss to follow up	1	16.7%	5	11.1%	1	25.0%	7	2.658	0.850
	Improved partially	0	0.0%	4	8.9%	0	0.0%	4		
	Death	1	16.7%	1	2.2%	0	0.0%	2		
	Worsened	0	0.0%	1	2.2%	0	0.0%	1		
Total		6	100.0%	45	100.0%	4	100.0%	55		

Figure 16: Distribution according to outcome and outcome diagnosis at 2 months follow up

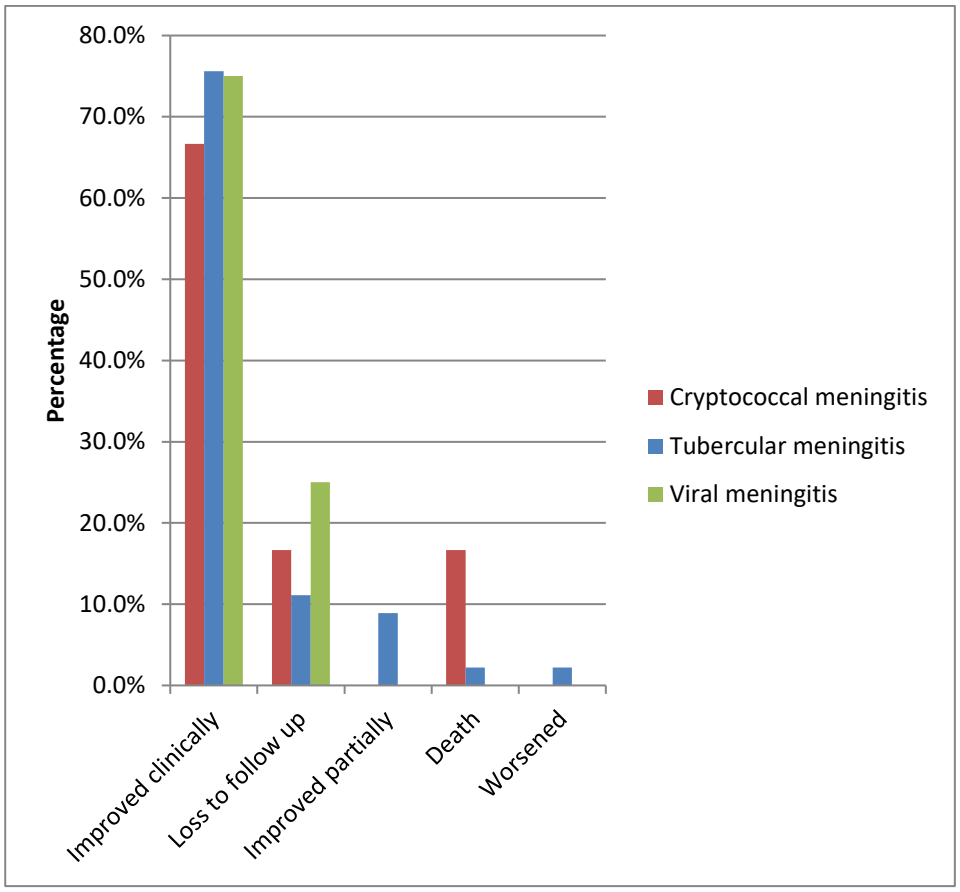


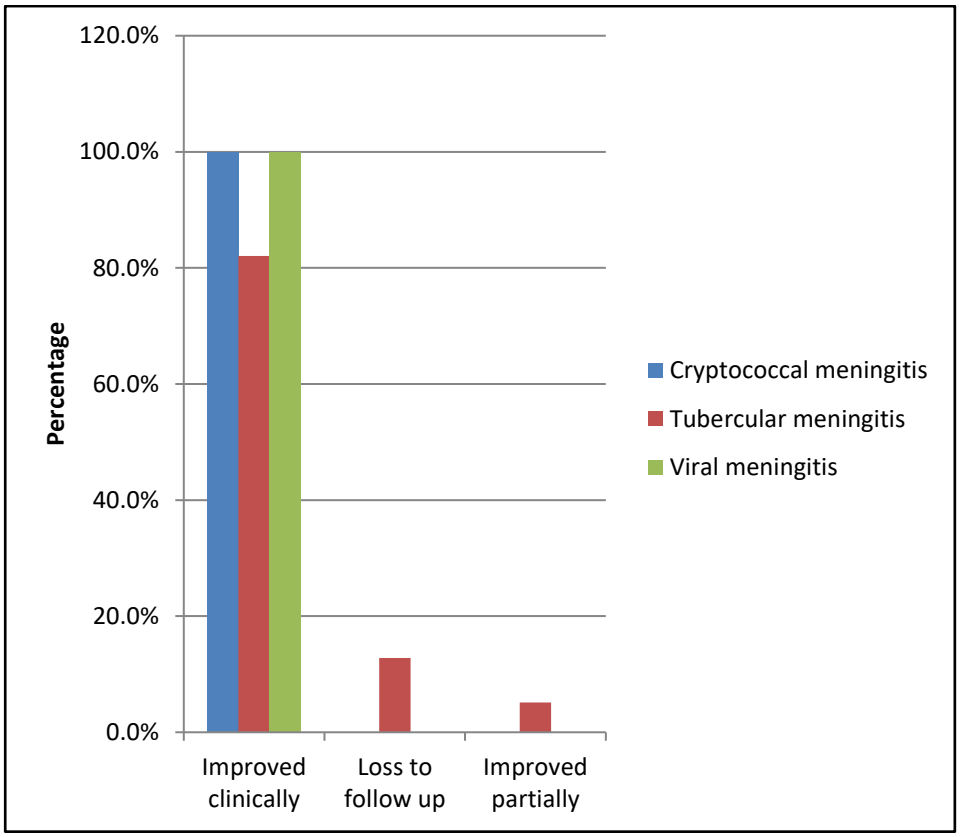
Table 33: Distribution according to outcome at 4 months follow up

						Total	Chi-square value	p-value
		No. of cases	Subacute (n=46)	No. of cases	Chronic (n=9)			
	Improved clinically	32	69.6%	7	77.8%	39		
	Improved partially	2	4.3%	0	0.0%	2		
4 months (improved cilinically/improved partially/worsened)	Loss to Follow up	12	26.1%	2	22.2%	14	0.507	0.776
Total		46	100.0%	9	100.0%	55		

Table 34: Distribution according to outcome diagnosis and outcome at 4 months follow up

		Outcome Diagnosis						Total	Chi-square value	p-value
		Cryptococcal meningitis		Tubercular meningitis		Viral meningitis				
4 Months (Improved clinically/Improved Partially/Worsened)	Improved clinically	4	100.0%	32	82.1%	3	100.0%	39	1.482	0.830
	Loss to follow up	0	0.0%	5	12.8%	0	0.0%	5		
	Improved partially	0	0.0%	2	5.1%	0	0.0%	2		
Total		4	100.0%	39	100.0%	3	100.0%	46		

Figure 17: Distribution according to outcome diagnosis and outcome at 4 months follow up



DISCUSSION

We conducted a prospective and observational study on patients admitted due to subacute and chronic meningitis in department of medicine and other allied specialties. It was carried over a period of 12 months from March 2021 to February 2022 at DMCH Ludhiana. It included 55 patients as per the inclusion criteria.

All these 55 patients were studied and evaluated as per protocol and underwent clinical examination and laboratory investigations.

Etiology, epidemiology, signs and symptoms, imaging findings, and treatment choices were recorded and evaluated. Symptoms were broad but altered sensorium, fever headache, nausea and vomiting were the most prevalent symptoms. Nuchal rigidity and cranial nerve palsies were the most common detected signs.

Among 55 patients, 46 patients had subacute onset illness. Of these,37 patients were diagnosed as tuberculous meningitis, 5 patients had cryptococcal meningitis and 4 patients had viral meningitis.

As Sulaiman et al. demonstrated, subacute meningitis tends to be higher in immunosuppressed patients than acute meningitis. They declared that age > 65, neurological symptoms in both acute and subacute, and fever in acute meningitis are associated with poor outcomes.[13] Our study revealed higher CSF leukocyte counts in subacute cases compared to chronic cases. No significant difference was detected in age, gender, and radiological findings.

In our study, there were total 9 cases of chronic meningitis. 8 were tubercular and 1 was fungal. A retrospective review of 49 patients with chronic idiopathic meningitis evaluated at Mayo Clinic identified an

etiology in 10 patients, with 8 of the 10 having a neoplastic cause. Overall, 24% of brain biopsies in this population yielded a diagnosis. Of the 39 undiagnosed cases, 85% of patients had a good outcome despite a prolonged illness. Corticosteroid therapy was effective in 52% of the patients treated but did not influence the outcome.[50] In those cases where history, examination, CSF analysis, novel testing, and biopsy fail to yield answers, clinicians may choose to offer empiric steroids.

In our study 31(56.4%) were males and 24(43.6%) were females with mean age of 44.7 years (range 18–80 years). In a study conducted by Bineshfar et al on 79 patients, the mean age was 37.3 years (range 6–95 years, median 33 years). Of these, 53 (67.1%) were males and 26 (32.9%) were females.[51]

The common presenting symptoms were altered sensorium (74.5%), fever (69.1%), Headache (38.2%) ,vomiting (40.0%) and seizure (21.8%) Among 55 patients with meningitis, 17 patients did not have fever during the course of illness.;17 patients did not have neck stiffness at all. This indicates that absence of fever or neck stiffness does not exclude the possibility of infectious meningitis.

A study conducted by Bineshfar et al showed that most common symptoms were headache (87.3%), nausea and vomiting (74.7%), fever (56.4%) and visual impairments (55.7%).[51]

In a study done by Bineshfar et al, they had a 44.3% definite diagnosis with bacterial (n:25, 31.6%) and neoplastic (n:8, 10.1%) being the most prevalent etiologies. *Mycobacterium tuberculosis* (60%) and *Brucella spp.* 12% were the most prevalent bacterial pathogens.[51].

M. tuberculosis and *cryptococcus neoformans* were common pathogens in our study.

Although the most commonly encountered opportunistic central nervous system (CNS) infections in AIDS patients are *Toxoplasma gondii, JC virus, Cryptococcus neoformans* and *cytomegalovirus.*[52] in AIDS

patients with chronic or subacute meningitis, TB still should be considered, especially in developing countries. In our study, there were total 9 HIV reactive patients,5 had cryptococcal meningitis,3 had tubercular meningitis and 1 had viral meningitis.

As Cherian et al. demonstrated, TB as an important infectious cause of chronic meningitis. The CSF analysis and neuroimaging may be negative, and test repetition is needed. Also, they suggest using GeneXpert/LPA and BACTEC to confirm the diagnosis. Although they declared that a negative result for these tests, does not rule out TB.[53] Therefore, empirical therapy with TB treatment and corticosteroids seems to be a reasonable choice in suspicious cases.

With repeated sequential examination of CSF, Kennedy and Fallon reported tubercle bacilli in 87% of patients. In their study, AFB were visible in stained CSF sediments in 37% patients during initial examinations, but the yield was 87% when the CSF from four serial spinal taps was examined.[54]

In another study bacteriological diagnosis was made in 107 of 132 adults in clinically suspected TBM. To increase the protein yield, a centrifuged sediment of more than 10 ml of CSF should be used for acid fast staining and 200-500 high power fields should be examined of each specimen for atleast 30 minutes, preferably by more than one observer. Serial CSF examination and examination of ventricular CSF will increase the yield further. (55) The sensitivity of CSF PCR testing was only 60% in patients classified as having definite or probable TM. [56] In another meta-analysis of PCR assay in TBM, the sensitivity was 56% and specificity was 98%.[57] In our study, CBNAAT was positive in 22 cases (40%).

Adenosine deaminase level was clearly higher in patients with tuberculous meningitis in our study, consistent with various earlier studies.[58,59] The mean value was found to be 22.

Gupta et al [60] observed that adenosine deaminase levels in nontuberculous disease rarely exceeded the cut-off; set for tuberculous disease(10U/L). They [48] have further observed that ADA estimation is not only a fairly sensitive and specific test (more than 90 %), helpful in differentiating tubercular from non-tubercular etiology; both in pulmonary and extra-pulmonary disease but is also simple, inexpensive and rapid. For this reason this test may help in early diagnosis, improve the prognosis and reduce spread of disease and sequelae.

Rana et al took 10 U/L as cutoff value for diagnosis of TBM and found sensitivity 66.6% and specificity 90%.[61] Baheti et al found that CSF ADA may differentiate tuberculous from non-tuberculous meningitis even at a cut-off level of 6.5 U/L [62]

In neurobrucellosis, another important cause of chronic meningitis, Dar et al. study showed CSF routine analysis and neuroimaging could be normal, and serology tests and tracing antibodies are needed to confirm the diagnosis.[63]

A case series of 114 patients diagnosed with chronic meningitis in Thailand found *C.neoformans* to be the most common causative agent (54%).[64] Seventy-nine percent of patients with *C neoformans* were HIV-positive. The second most common cause of chronic meningitis in this case series was *M tuberculosis* (37%).64]

A case report published in 2005 discussed the difficulty of diagnosing chronic meningitis in a patient who had capsule-deficient *C neoformans*.[44] It is important to consider this possibility when antigen tests are negative but strong suspicion of chronic meningitis exists.

In our study 6 patients had cryptococcal meningitis; 5 patients had HIV infection. The one patient without HIV infection was diabetic. CSF analysis revealed positive cryptococcal antigen and he was started on amphotericin B and high dose IV fluconazole. Patient improved

gradually. The patient with HIV infection and cryptococcal meningitis recovered well with amphotericin.

In a study done by Pandey et al in 356 patients, there were three confirmed cases of fungal meningitis. The mean value of TLC was 11.7 cells/mm3 with lymphocytic predominance. In fungal meningitis glucose level was found to be normal (45.0 mg/dL) with slight increase in protein (48.7 mg/dL).[65] In our study, mean value of TLC in fungal meningitis was 62.33 cells/mm^3 with lymphocytic predominance. Mean protein was 153.28 mg/dl and mean glucose was 50.73 mg/dl.

In imaging modalities, hydrocephalus on CT scan and leptomeningeal enhancement and hydrocephalus on MRI were recorded in several patients. The sensitivity and specificity of CT scan and MRI in subacute and chronic meningitis were lower early in the course of the disease compared to acute meningitis and could vary based on the etiology and timeline of the disease period.[66]

In our study 18 patients (32.7%) had basal meningeal exudates in brain imaging (MRI Brain). Few patients underwent only CT scan which revealed basal meningeal enhancement. Hydrocephalus was present in 10 patients (18.2%). Only 2 patients had significantly larger hydrocephalus, progressively increasing in size and underwent VP shunt. Vasculitic infarcts were present in 2 patients (3.6%) and granulomas were present in 4 patients (7.3%).

In study conducted by Bineshfar et al, it showed that Brain CT was normal in 68.6% of patients, while hydrocephalus was found in 22.9% of cases. Brain MRI was normal in 60.0% of the patients. The most common abnormal MRI findings were leptomeningeal enhancement (16.0%) and hydrocephalus (16.0%).

In two large community based series, hydrocephalus was seen in approximately 75% of patients, basilar meningeal enhancement in 38%, cerebral infarcts in 15%-30% and tuberculomas in 5-10%. [67,68]

Sometimes the boundaries between acute and chronic meningitis become indistinguishable. Infectious etiologies of acute meningitis may unexpectedly result in subacute or chronic meningitis. Lefevre et al. demonstrated that *Neisseria meningitidis* can result in chronic meningitis, which mainly presents with fever, rash, and arthralgia in young male patients [69].

Tabaja et al. showed VZV could cause both encephalitis and meningitis. Meningitis is more expected in younger populations. [70]

Subacute and chronic listeriotic meningitis are thought to typically occur in immunocompromised patients, but as reported by Arslan et al., immunocompetent patients developed listeriosis meningitis with a course of more than seven days.[71]

Mandal et al. declared that the preceding use of antibiotics could affect the CSF analysis results. However, they believed that limited use of some oral agents did not significantly impact CSF analysis and diagnostic approaches. A history of two weeks of antibiotic use for otitis media prior to admission, and a history of corticosteroid use were noticed in the two patients with *Streptococcus pneumoniae* subacute meningitis. Antibiotics did not affect the results of CSF culture, but they may be the cause of uncommon presentation of a typical acute meningitis etiology. Moreover, in this patient the symptoms could be attributed to severe acute otitis media instead of meningitis. Thus, common acute meningitis etiologies can cause subacute and chronic meningitis due to previous use of antibiotics or corticosteroids.[72]

An individual approach for diagnosing and treating subacute and chronic meningitis is suggested. TBM rate is high in particular areas, especially in low-income patients. Therefore, geographic epidemiology and socioeconomic situation should be considered in the differential diagnosis of chronic meningitis. Etiologic pathogens of acute meningitis can cause subacute and chronic meningitis in some patients.[51]

SUMMARY AND CONCLUSION

1. Patients were divided into two groups based on duration of illness- 5-30 days-Sub acute meningitis and >30 days-Chronic meningitis.

2. In this study, most of the patients with meningitis were males and young adults.

3. Tuberculous meningitis was the most common overall cause in this study.

4. The most common symptoms were altered sensorium (74.5%), fever (69.1%), headache (38.2%), vomiting (40%), seizure (12%) .

5. The most common signs were neck rigidity (69.1%) and cranial nerve palsy (9.1%). Most common cranial nerve involved was 6^{th} nerve.

6. Tuberculous meningitis was the most common cause in patients with subacute meningitis. Diagnosis of tuberculous meningitis was challenging; clinical presentation, CSF studies, and brain imaging features helped to make a diagnosis of tuberculous meningitis.

7. The most common MRI findings were Meningeal enhancement (32.7%), hydrocephalus (18.2%), vasculitic infarcts (3.6%), granulomas (7.3%)

8. We came across atypical presentation of cryptococcal meningitis in a non-HIV patient who was diabetic.

9. Most of the cases improved clinically after appropriate treatment.

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S.NO	MRD NO	NAME	AGE	AGE GROUP	GENDER	DOA	DOD	DISCHARGE	DEATH	DAMA	DOR	LENGTH OF STAY IN WARD (IN DAYS)	LENGTH OF STAY IN ICU (IN DAYS)	OUTCOME DIAGNOSIS	CHIEF COMPLAINTS	DURATION OF ILLNESS
1	957960	JG	37	1	M	30.03.2021	07.04.2021	YES	NO	NO	NO	8	0	CRYPTOCOCCAL MENINGITIS		5-30 DAYS
2	1100341	LS	18	0	F	30.04.2021	10.05.2021	YES	NO	NO	NO	9	2	TUBERCULAR MENINGITIS		5-30 DAYS
3	993575	HS	55	3	M	02.04.2021	06.04.2021	NO	NO	NO	YES	5	0	TUBERCULAR MENINGITIS		5-30 DAYS
4	1096263	SK	75	4	F	26.04.2021	04.05.2021	YES	NO	NO	NO	8	0	TUBERCULAR MENINGITIS		5-30 DAYS
5	1078145	HS	26	0	M	03.06.2021	14.06.2021	YES	NO	NO	NO	9	2	CRYPTOCOCCAL MENINGITIS		5-30 DAYS
6	1071072	GS	46	2	M	26.06.2021	20.07.2021	NO	NO	YES	NO	16	10	TUBERCULAR MENINGITIS		5-30 DAYS
7	1026075	MEGHA	34	1	F	04.04.2021	09.04.2021	YES	NO	NO	NO	4	1	TUBERCULAR MENINGITIS		5-30 DAYS
8	1122876	PB	37	1	F	15.06.2021	21.06.2021	YES	NO	NO	NO	3	4	TUBERCULAR MENINGITIS		5-30 DAYS
9	1128159	HSW	33	1	M	26.06.2021	15.07.2021	YES	NO	NO	NO	8	1	TUBERCULAR MENINGITIS		5-30 DAYS
10	1130196	DS	80	4	M	01.07.2021	10.07.2021	NO	NO	NO	YES	4	6	TUBERCULAR MENINGITIS		5-30 DAYS
11	1120986	MY	53	3	M	24.07.2021	30.07.2021	YES	NO	NO	NO	5	1	TUBERCULAR MENINGITIS		5-30 DAYS
12	1174807	MK	36	1	F	16.09.2021	30.09.2021	NO	NO	NO	YES	12	3	TUBERCULAR MENINGITIS		5-30 DAYS
13	1199666	KD	70	4	F	29.10.2021	05.11.2021	YES	NO	NO	NO	4	3	TUBERCULAR MENINGITIS		5-30 DAYS
14	1186789	SS	50	2	M	07.10.2021	14.10.2021	YES	NO	NO	NO	5	3	TUBERCULAR MENINGITIS		5-30 DAYS
15	1193409	MB	58	3	F	18.10.2021	06.11.2021	YES	NO	NO	NO	20	20	VIRAL MENINGITIS		5-30 DAYS
16	1147766	KR	70	4	F	03.08.2021	14.08.2021	YES	NO	NO	NO	10	2	TUBERCULAR MENINGITIS		5-30 DAYS
17	1175503	JS	36	1	M	18.09.2021	30.09.2021	YES	NO	NO	NO	8	4	CRYPTOCOCCAL MENINGITIS		5-30 DAYS
18	1186117	DC	68	4	M	05.10.2021	14.10.2021	YES	NO	NO	NO	6	3	TUBERCULAR MENINGITIS		>30 DAYS
19	1187369	MS	40	1	M	08.10.2021	12.10.2021	NO	NO	YES	NO	0	4	CRYPTOCOCCAL MENINGITIS		5-30 DAYS
20	1178346	KK	37	1	F	22.09.2021	09.10.2021	YES	NO	NO	NO	17	0	VIRAL MENINGITIS		5-30 DAYS
21	1174807	MK	36	1	F	16.09.2021	30.09.2021	NO	NO	NO	YES	5	10	TUBERCULAR MENINGITIS		5-30 DAYS
22	1208053	NEHA	30	0	F	15.11.2021	20.11.2021	NO	NO	NO	YES	3	3	TUBERCULAR MENINGITIS		5-30 DAYS
23	1203386	FA	58	3	M	27.06.2021	30.06.2021	YES	NO	NO	NO	4	0	TUBERCULAR MENINGITIS		>30 DAYS
24	1208893	JK	27	0	F	25.06.2021	10.07.2021	YES	NO	NO	NO	13	2	TUBERCULAR MENINGITIS		5-30 DAYS
25	1209911	SB	46	2	F	24.07.2021	30.07.2021	YES	NO	NO	NO	6	0	TUBERCULAR MENINGITIS		5-30 DAYS
26	1197953	LAK	31	1	M	26.10.2021	30.10.2021	YES	NO	NO	NO	4	0	TUBERCULAR MENINGITIS		>30 DAYS
27	1176257	HARI	46	2	M	08.08.2021	15.08.2021	YES	NO	NO	NO	7	0	TUBERCULAR MENINGITIS		5-30 DAYS
28	1220890	AK	30	0	F	08.12.2021	21.12.2021	NO	NO	YES	NO	0	13	TUBERCULAR MENINGITIS		5-30 DAYS
29	1218277	RK	62	4	F	04.12.2021	27.12.2021	YES	NO	NO	NO	5	18	TUBERCULAR MENINGITIS		5-30 DAYS
30	1154139	SK	49	2	F	13.08.2021	30.08.2021	YES	NO	NO	NO	7	10	TUBERCULAR MENINGITIS		5-30 DAYS
31	1186117	DS	68	4	M	17.11.2021	05.12.2021	NO	NO	NO	YES	0	18	TUBERCULAR MENINGITIS		5-30 DAYS
32	1230292	SR	70	4	F	27.12.2021	06.01.2022	YES	NO	NO	NO	5	6	TUBERCULAR MENINGITIS		5-30 DAYS
33	1046155	SKB	52	3	M	19.12.2021	07.01.2022	NO	NO	YES	NO	12	7	TUBERCULAR MENINGITIS		>30 DAYS
34	477204	SS	78	4	M	03.12.2021	11.12.2021	YES	NO	NO	NO	8	0	TUBERCULAR MENINGITIS		5-30 DAYS

ALTERED SENSORIUM	DURATION(DAYS)	FEVER	DURATION(DAYS)	HEADACHE	DURATION (DAYS)	SEIZURE	TYPE	VOMITING	DURATION(DAYS)	PAST HISTORY	DIABETES MELLITUS	TUBERCULOSIS	TRAUMA	SEIZURE DISORDER	DRUG HISTORY	ANTI TUBERCULAR	ANTI EPILEPTIC	SENSORIUM
NO		YES	5	NO		YES	GTCS	NO			NO	NO	NO	NO		NO	NO	CONSCIOUS
YES	3	NO		NO		NO		YES	5		NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	5	NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	2	YES	6	NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	1	NO		YES	6	NO		NO			NO	NO	NO	NO		ATT	NO	ALTERED
NO		YES	7	NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	2	YES	6	NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	1	NO		YES	7	NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
NO		YES	2	YES	7	NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	4	NO		NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	1	NO		YES	5	NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	5	YES	10	NO		NO		YES	1		NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	5	NO		NO		YES	1		NO	NO	NO	NO		NO	NO	ALTERED
YES	2	NO		NO		YES		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	20	YES	20	NO		NO		NO			YES	NO	NO	NO		NO	NO	ALTERED
YES	2	NO		NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	2	NO		YES	15	NO		YES	4		NO	NO	NO	NO		NO	NO	CONSCIOUS
YES	2	NO		NO		NO		YES	2 MONTH		YES	NO	NO	NO		NO	NO	ALTERED
NO		NO		YES	7	YES	GTCS, LEPISODE	YES	7		NO	NO	NO	NO		YES	NO	ALTERED
NO		YES	8	YES	7	NO		YES	4		NO	NO	NO	NO		NO	NO	ALTERED
YES	1	NO		YES	10	NO		YES	4		NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	7	NO		NO		YES	3		NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	1 MONTH	NO		NO		YES	4		NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	10	NO		YES	GTCS	NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	2	NO		YES		YES	3		NO	NO	NO	NO		NO	NO	ALTERED
NO		YES	1 MONTH	YES	1 MONTH	NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	7	YES	10	NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	10	YES	6	NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	2	YES	7	NO		NO		YES	4		NO	NO	NO	NO		NO	NO	ALTERED
YES	4	YES	10 TO 12	YES	10	YES	GTCS	YES	10		NO	NO	NO	NO		NO	NO	ALTERED
YES	6	NO		NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	10	NO		NO		YES			YES	NO	NO	NO		NO	NO	ALTERED
YES	1	NO		YES	1 MONTH	YES	GTCS	NO			NO	NO	NO	NO		NO	NO	ALTERED
YES		NO		NO		YES		YES	3		NO	NO	NO	NO		NO	NO	ALTERED

GCS	PULSE(/MIN.)	SBP	DBP	TEMPERATURE(F)	NECK RIGIDITY	CRANIAL NERVE PALSY	FUNDUS	TLC(ADM) X10^3	TLC(DIS) X10^3	ESR(ADM)	TOTAL BIL (ADM)	TOTAL BIL (DIS)	SGOT(ADM)	SGOT(DIS)
15	88	110	80	98.7	NO	NORMAL		10	11.5	50	0.25	0.48	40	51
13	85	130	80	98.6	NO	RT 3RD NERVE, LT 6TH NERVE	PAPILLEDEMA	12.9	15	55	0.92		13	11
13	85	140	80	98.3	YES	NORMAL		6.1		50	0.64		40	
13	80	130	70	99.5	YES	NORMAL		6.8	7.8	30	0.42	0.39	55	56
13	80	130	80	98.6	YES	NORMAL		13.1	22.4		1.68	1.02	74	892
3	100	120	80	100	YES	NORMAL	CHOROID TUBERCLES	11.3	20.3	40	0.63	0.56	40	90
14	90	110	70	98.6	YES	NORMAL		10	9	40	0.64	0.7	40	34
13	94	120	70	99	YES	NORMAL		6.6		40	0.61		18	24
14	90	122	84	99.8	YES	NORMAL	PAPILLEDEMA	12.6			0.25		34	
12	82	110	76	98.3	YES	RT 7TH NERVE PALSY		14.7	15	40	1.41	1.2	61	70
13	80	120	70	99	YES	NORMAL		10		86	0.53		40	
12	60	120	70	98.7	YES	NORMAL		12		60			49	60
12	90	136	78	99	YES	NORMAL		14.2	10.3	57	0.87		23	20
15	100	110	70	99.6	YES	NORMAL	CHOROID TUBERCLES	5.5	6.6	120	1.29	1.2	37	32
15	90	120	70	99.4	YES	NORMAL		10.7	7.7	69	0.4	0.16	34	20
13	74	110	70	99.9	YES	NORMAL		7.2	14.5	48	0.57	0.51	23	18
15	60	100	60	99.2	YES	NORMAL		5.2	5.5	59	0.42		57	
15	80	120	80	100	YES	NORMAL		16.4	9.5	10	1		45	40
15	75	110	70	98.8	NO	RT 6TH NERVE PALSY	PAPILLEDEMA	9.1	9.3	25	3.95		63	
15	80	110	70	99.5	YES	NORMAL		4.3			1.57		30	
15	90	120	70	99.1	YES	NORMAL	PAPILLEDEMA	16.1	16.7		0.67		16	
13	90	130	70	100.2	YES	NORMAL		20.5	13.4	56	0.73		21	11
12	98	130	70	99.4	YES	NORMAL		19.2	8.8	46	0.54	0.23	107	127
10	92	110	70	99.6	YES	NORMAL		22.4	10.4	55	0.18	0.78	36	45
14	69	130	70	99.3	NO	NORMAL		10.7	7.2		0.24	0.3	40	42
15	90	120	70	99	NO	NORMAL		15.5		60	0.93		64	
14	90	126	72	99.2	YES	NORMAL		11.1			0.46		48	
11	90	120	70	100.3	YES	NORMAL		19.2	14.2	20	0.73		41	
14	90	140	80	99.4	YES	NORMAL		7.7	9	30	0.22	0.47	35	148
14	94	120	70	99.6	YES	NORMAL	PAPILLEDEMA	7.6	8	48	0.24	0.45	45	40
14	90	130	80	99.9	YES	NORMAL		10	11	30	0.4	0.6	40	50
14	60	120	70	99.3	YES	NORMAL		15	6	63	0.63		27	
7	100	100	60	99.5	NO	NORMAL		9.13	8.77	81	0.3		28	23
15	100	120	70	99.4	YES	NORMAL		11.2		20	0.93	0.43	23	31

SGPT(ADM)	SGPT(DIS)	VIRAL MARKERS (HIV/HCV/HBSAg)	CSF	PROTEIN	GLUCOSE	CHLORIDE	TLC	MNC	NEUTROPHILS	GRAM STAIN	CULTURE	CBNAAT	AFB	ADA	CRYPTOCOCCAL	HSV	MRI FINDINGS
40	53	HIV		120	40	100	10	90	10	NEG	NEG	NEG	NEG	10	POSITIVE	NEGATIVE	
8	11	NR		82.9	19	106	100	100	0	NEG	NEG	DETECTED	NEG	6.7	NEGATIVE	NEGATIVE	HYDROCEPHALUS,MENINGEAL ENHANCEMENT
45		NR		120	30	100	20	100	0	NEG	NEG	DETECTED	NEG	24	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT,VASCULITIC INFARCTS
112	160	NR		157.2	47	115	400	85	15	NEG	NEG	NEG	NEG	19.2	NEGATIVE	NEGATIVE	HYDROCEPHALUS
64	691	HIV		458.4	47	133	100	40	60	NEG	NEG	NEG	NEG	9.4	POSITIVE	NEGATIVE	
44	96	NR		66	70	115	10	60	40	NEG	NEG	DETECTED	NEG	40.9	NEGATIVE	NEGATIVE	VASCULITIC INFARCTS,GRANULOMAS
34	32	NR		99	120	100	40	90	10	NEG	NEG	DETECTED	NEG		NEGATIVE	NEGATIVE	
18	24	NR		188.6	58	112	200	90	10	NEG	NEG	NEG	NEG	12.5	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT,GRANULOMAS
55		NR		67.3	19	112	38	70	30	NEG	NEG	NEG	NEG	11.2	NEGATIVE	NEGATIVE	HYDROCEPHALUS,GRANULOMAS
36	70	NR		232.3	64	125	85	100	0	NEG	NEG	DETECTED	TRACES	0	NEGATIVE	NEGATIVE	
40		NR		120	30	100	30	95	5	NEG	NEG	DETECTED	NEG	2	NEGATIVE	NEGATIVE	
40	62	NR		130.8	85	129	240	30	70	NEG	NEG	NEG	NEG	15	NEGATIVE	NEGATIVE	
15	31	NR		252.7	16	121	70	70	30	NEG	NEG	NEG	NEG	39.6	NEGATIVE	NEGATIVE	
28	24	HIV		60	40	100	10	90	10	NEG	NEG	DETECTED	NEG	9.3	NEGATIVE	NEGATIVE	GRANULOMAS
18	16	NR		56.8	110	117	12.5	100	0	NEG	NEG	NEG	NEG	14.7	NEGATIVE	NEGATIVE	
9	21	NR		57.1	77	122	100	100	0	NEG	NEG	NEG	NEG	1.64	NEGATIVE	NEGATIVE	
66		HIV, HCV		39.2	51	117	200	98	2	NEG	NEG	NEG	NEG	20.7	POSITIVE	NEGATIVE	
88	40	NR		49.4	79	109	25	100	0	NEG	NEG	NEG	NEG	1.72	NEGATIVE	NEGATIVE	
36		HIV		83.9	19	116	5	95	5	NEG	NEG	NEG	NEG	11.2	POSITIVE	NEGATIVE	HYDROCEPHALUS
27		HIV		94.8	47	127	25	90	10	NEG	NEG	NEG	NEG	11.2	NEGATIVE	POSITIVE	
19		NR		130.8	25	129	240	70	30	NEG	NEG	NEG	NEG	13.6	NEGATIVE	NEGATIVE	HYDROCEPHALUS
31	13	NR		154.1	53	112	8	100	0	NEG	NEG	DETECTED	NEG	14.9	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
33	119	NR		63	10	130	6	100	0	NEG	NEG	DETECTED	NEG	16.83	NEGATIVE	NEGATIVE	
50	32	HCV		79.2	25	138	28	90	10	NEG	NEG	NEG	NEG	0.34	NEGATIVE	NEGATIVE	
51	42	NR		67.7	30	126	5	100	0	NEG	NEG	DETECTED	NEG	30	NEGATIVE	NEGATIVE	
128		NR		79	15	111	70	100	0	NEG	NEG	NEG	NEG	11.8	NEGATIVE	NEGATIVE	
97		NR		76.7	10	113	300	20	80	NEG	NEG	DETECTED	NEG	19.7	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
45		NR		55.6	74	145	5	100	0	NEG	NEG	DETECTED	NEG	29	NEGATIVE	NEGATIVE	
7	223	NR		60	40	122	6	100	0	NEG	NEG	DETECTED	NEG	30	NEGATIVE	NEGATIVE	
50	45	NR		120	28	100	200	90	10	NEG	NEG	NEG	NEG	20	NEGATIVE	NEGATIVE	HYDROCEPHALUS
45	51	NR		70	30	100	18	100	0	NEG	NEG	DETECTED	NEG	13.7	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
34		NR		209	25	27	80	90	10	NEG	NEG	DETECTED	NEG	15.3	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
31	25	HIV		202.1	34	124	45	100	0	NEG	NEG	DETECTED	NEG	31.5	NEGATIVE	NEGATIVE	
21	13	NR		39.6	111	124	5	100	0	NEG	NEG	NEG	NEG	9.23	NEGATIVE	NEGATIVE	

HYDROCEPHALUS	MENINGEAL ENHANCEMENT	VASCULITIC INFARCTS	GRANULOMAS	FOLLOW UP	LOSS TO FOLLOW UP	2 MONTH (IMPROVED CILINICALLY/IMPROVED PARTIALLY/WORSENED/EXPIRED)	4 MONTH (IMPROVED CILINICALLY/IMPROVED PARTIALLY/WORSENED/EXPIRED)
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
YES	YES					IMPROVED CILINICALLY	IMPROVED CLINICALLY
	YES	YES				IMPROVED CILINICALLY	IMPROVED CLINICALLY
YES						IMPROVED CILINICALLY	IMPROVED CLINICALLY
					YES		
		YES	YES		YES		
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
	YES		YES			IMPROVED CILINICALLY	IMPROVED CLINICALLY
YES			YES			IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED PARTIALLY	IMPROVED PARTIALLY
						WORSENED	
			YES			IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
YES					YES	EXPIRED	
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
YES						IMPROVED CILINICALLY	IMPROVED CLINICALLY
	YES					IMPROVED PARTIALLY	IMPROVED PARTIALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
	YES					IMPROVED CILINICALLY	
					YES		
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
YES						IMPROVED CILINICALLY	IMPROVED CLINICALLY
	YES					IMPROVED CILINICALLY	
	YES					IMPROVED CILINICALLY	IMPROVED CLINICALLY
					YES		
						IMPROVED CILINICALLY	IMPROVED CLINICALLY

35	1217874	BS	30	0	M	03.12.2021	20.12.2021	YES	NO	NO	NO	17	0	CRYPTOCOCCAL MENINGITIS		>30 DAYS
36	1251378	ND	45	2	F	09.02.2022	17.02.2022	NO	NO	YES	NO	8	0	VIRAL MENINGITIS		5-30 DAYS
37	1256943	AV	53	3	M	21.02.2022	28.02.2022	YES	NO	NO	NO	6	2	CRYPTOCOCCAL MENINGITIS		5-30 DAYS
38	1192583	MR	50	2	F	17.10.2021	29.10.2021	NO	NO	YES	NO	12	0	TUBERCULAR MENINGITIS		5-30 DAYS
39	1227060	KD	58	3	F	21.12.2021	01.01.2022	YES	NO	NO	NO	1	10	TUBERCULAR MENINGITIS		5-30 DAYS
40	1243057	SS	28	0	M	21.10.2021	29.10.2021	YES	NO	NO	NO			TUBERCULAR MENINGITIS		5-30 DAYS
41	1249500	DS	55	3	M	06.02.2022	22.02.2022	NO	NO	YES	NO	0	17	TUBERCULAR MENINGITIS		5-30 DAYS
42	1229529	PG	42	2	F	25.12.2021	27.12.2021	NO	NO	NO	YES	2	0	TUBERCULAR MENINGITIS		5-30 DAYS
43	1251405	PR	30	0	F	10.02.2022	19.02.2022	YES	NO	NO	NO	8	1	TUBERCULAR MENINGITIS		5-30 DAYS
44	1259542	KS	30	0	M	24.02.2022	07.03.2022	YES	NO	NO	NO	8	3	TUBERCULAR MENINGITIS		>30 DAYS
45	1243260	BS	21	0	M	23.01.2022	29.01.2022	YES	NO	NO	NO	0	6	TUBERCULAR MENINGITIS		5-30 DAYS
46	1242126	RB	45	2	M	20.01.2022	24.01.2022	YES	NO	NO	NO	5	0	VIRAL MENINGITIS		5-30 DAYS
47	1250011	PALAK	26	0	F	07.02.2022	13.02.2022	NO	NO	NO	YES	6	0	TUBERCULAR MENINGITIS		5-30 DAYS
48	1129994	HS	45	2	M	30.06.2021	15.07.2021	YES	NO	NO	NO	6	10	TUBERCULAR MENINGITIS		5-30 DAYS
49	1077944	SS	62	4	M	08.04.2021	12.04.2021	YES	NO	NO	NO	0	4	TUBERCULAR MENINGITIS		5-30 DAYS
50	1118376	RS	35	1	M	07.06.2021	09.06.2021	NO	NO	YES	NO	0	2	TUBERCULAR MENINGITIS		5-30 DAYS
51	406846	RS	34	1	M	22.07.2022	25.07.2022	NO	NO	NO	YES	4	0	TUBERCULAR MENINGITIS		5-30 DAYS
52	1146155	RS	23	0	M	31.07.2021	09.08.2021	NO	NO	NO	YES	7	2	TUBERCULAR MENINGITIS		>30 DAYS
53	1147597	NAMAN	18	0	M	03.08.2021	27.08.2021	YES	NO	NO	NO	0	24	TUBERCULAR MENINGITIS		>30 DAYS
54	1146447	AJ	22	0	F	01.08.2021	09.08.2021	YES	NO	NO	NO	8	0	TUBERCULAR MENINGITIS		>30 DAYS
55	9555470	BD	67	4	M	27.07.2021	10.08.2021	YES	NO	NO	NO	5	9	TUBERCULAR MENINGITIS		5-30 DAYS

NO		YES	2 MONTTH	YES	1	NO		YES	2		NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	15 TO 20	NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	3 TO 4	YES	8 TO 9	NO		NO			YES	NO	NO	NO		NO	NO	ALTERED
YES	4	YES	10	NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
NO		YES	15	YES	15	NO		YES	3		NO	NO	NO	NO		NO	NO	ALTERED
NO		YES	15	YES	10	NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	15	NO		NO		YES	GTCS	NO			YES	NO	NO	NO		NO	NO	ALTERED
YES	2	NO		YES	30	NO		YES	10		NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	4	YES	4	NO		YES	3		NO	NO	NO	NO		NO	NO	ALTERED
YES	3	YES	3 MONTH	NO		YES	GTCS	NO			NO	YES	NO	NO		YES	NO	ALTERED
YES	1	YES	5	YES	7	NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	1	NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
NO		YES	2	YES	10	NO		YES	4		NO	NO	NO	NO		NO	NO	ALTERED
YES	2	NO		NO		NO		YES	4		NO	NO	NO	NO		NO	NO	ALTERED
NO		YES	6	NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	2	YES	5	NO		YES	GTCS	NO			NO	NO	NO	NO		NO	NO	ALTERED
NO		YES	10	NO		YES	GTCS	YES	1		NO	NO	NO	NO		NO	NO	ALTERED
YES	2 TO 3	YES	1 MONTH	NO		NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
NO		YES	1.5 MONTH	YES	10	NO		NO			NO	YES	NO	NO		NO	NO	ALTERED
NO		YES	6 MONTH	YES	1 WEEK	NO		NO			NO	NO	NO	NO		NO	NO	ALTERED
YES	1	YES	10	NO		NO		NO			YES	NO	NO	NO		NO	NO	ALTERED

15	120	100	60	99.1	NO	NORMAL		6.6	3.3	33	1.02		123	
15	110	100	70	99.8	NO	NORMAL		7.2	7.4	30	0.46	0.57	43	58
14	90	110	70	100.1	YES	NORMAL	PAPILLEDEMA	9.3		12	0.91		29	
9	85	130	80	99	YES	NORMAL	PAPILLEDEMA	12.2	15.6	40	0.63	0.65	74	43
15	98	120	70	99.3	NO	NORMAL		7.7	9	40	0.24	0.47	35	40
15	90	110	70	98.9	YES	NORMAL		7.8	9	12	0.37	0.59	22	23
3	90	120	70	99	YES	NORMAL		4.7	16.4	63	0.4	0.63	71	89
15	90	120	70	99.2	NO	NORMAL	PAPILLEDEMA	10.1		33	0.36		19	
12	110	110	70	99.5	YES	NORMAL		10	13	32	0.29	0.7	110	224
12	86	100	60	99.1	NO	NORMAL	PAPILLEDEMA	11.4	9	30.7	0.66	0.4	43	40
14	100	110	70	99.7	NO	NORMAL		19	14.7				35	27
13	94	110	70	99.3	NO	NORMAL		6.6	6.6			0.49		10
15	90	110	70	99.6	YES	NORMAL		7.9	5.1	20	0.23		23	
14	90	120	80	100	YES	NORMAL		9.1	10.7	47	3.94	1.2	83	48
13	100	120	70	99.8	YES	NORMAL		6.6		45	0.42	0.43	45	27
14	110	120	70	99.4	YES	NORMAL		10.8	20.2		1.02	0.79	145	62
15	80	110	70	99.4	NO	NORMAL		5.65	7				64	
14	80	110	70	99.7	YES	NORMAL		17	23.8	36	0.55	1.45	32	29
13	89	110	70	99.5	NO	LT 6TH NERVE PALSY		9.5	8.2	60	0.49	0.35	67	59
15	92	110	90	99.3	NO	RT 6TH NERVE PALSY		7.9	9.2	47	0.69	0.68	49	32
10	72	160	100	99.2	NO	NORMAL		7	12.1	64	0.43	0.38	50	23

141		HIV		46.9	61	125	50	20	80	NEG	NEG	NEG	NEG	16.66	POSITIVE	NEGATIVE	
27	50	NR		288.6	6	109	15	70	30	NEG	NEG	NEG	NEG	18.9	NEGATIVE	NEGATIVE	
22		NR		171.3	86.4		9	100	0	NEG	NEG	NEG	NEG	5	POSITIVE	NEGATIVE	HYDROCEPHALUS
36	33	NR		120	34	100	100	90	10	NEG	NEG	DETECTED	NEG	20	NEGATIVE	NEGATIVE	HYDROCEPHALUS.MENINGEAL ENHANCEMENT
40	70	NR		95	49	110	210	95	5	NEG	NEG	DETECTED	NEG	11.5	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
82	84	NR		122.1	24	111	325	90	10	NEG	NEG	NEG	NEG	13.4	NEGATIVE	NEGATIVE	
99	135	NR		127	40	117	20	90	10	NEG	NEG	NEG	NEG	20	NEGATIVE	NEGATIVE	
15		NR		55	73	124	6	100	0	NEG	NEG	DETECTED	NEG	1.77	NEGATIVE	NEGATIVE	HYDROCEPHALUS,MENINGEAL ENHANCEMENT
239	561	NR		253	24	105	5	100	0	NEG	NEG	DETECTED	TRACES	23.5	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
67	45	NR		429	61	109	400	30	70	NEG	NEG	DETECTED	NEG	20	NEGATIVE	NEGATIVE	HYDROCEPHALUS,MENINGEAL ENHANCEMENT
81	45	HCV		116.9	17	106	25	95	5	NEG	NEG	DETECTED	NEG	12.4	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
	14	NR		47.5	60	121	20	90	10	NEG	NEG	NEG	NEG	0.88	NEGATIVE	POSITIVE	
10		NR		131.4	53	114	10	95	5	NEG	NEG	NEG	NEG	14.7	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
34	40	HIV, HCV		136.7	67	124	30	90	10	NEG	NEG	NEG	NEG	20	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
72	69	NR		120	40	100	30	80	20	NEG	NEG	NEG	NEG	20	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
273	226	NR		100.7	76	118	18	80	20	NEG	NEG	NEG	NEG	24	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
56		NR		123	39	117	10	80	20	NEG	NEG	NEG	NEG	20	NEGATIVE	NEGATIVE	
67	16	NR		89	42	119	200	60	40	NEG	NEG	NEG	NEG	24.7	NEGATIVE	NEGATIVE	MENINGEAL ENHANCEMENT
39	57	NR		148.4	31	118	60	100	0	NEG	NEG	NEG	NEG	100	NEGATIVE	NEGATIVE	
48	66	NR		73.5	42	122	90	90	10	NEG	NEG	NEG	NEG	152.5	NEGATIVE	NEGATIVE	
19	9	NR		123	39	117	30	100	0	NEG	NEG	NEG	NEG	30	NEGATIVE	NEGATIVE	

						IMPROVED CILINICALLY	IMPROVED CLINICALLY
					YES		
YES						IMPROVED CILINICALLY	IMPROVED CLINICALLY
YES	YES				YES	EXPIRED	
	YES					IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
					YES		
YES	YES					IMPROVED PARTIALLY	
	YES					IMPROVED CILINICALLY	IMPROVED CLINICALLY
YES	YES					IMPROVED CILINICALLY	IMPROVED CLINICALLY
	YES					IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
	YES					IMPROVED CILINICALLY	IMPROVED CLINICALLY
	YES					IMPROVED CILINICALLY	IMPROVED CLINICALLY
	YES					IMPROVED CILINICALLY	IMPROVED CLINICALLY
	YES				YES		
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
	YES					IMPROVED PARTIALLY	
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY
						IMPROVED CILINICALLY	IMPROVED CLINICALLY

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(28)

No. BFUHS/2K21p-TH/ 153 Date 05/01/22.

The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.10.2021 has approved the plan of thesis of **Shivika**, a student of your college for **MD General Medicine** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Spectrum and outcome in adult patients of subacute and chronic meningitis.

Supervisor
Dr. Gautam Ahluwalia
Prof.,
Dept. of Medicine,
DMCH, Ludhiana.

Co-Supervisor

Dr. Gagandeep Singh
Prof. & Head,
Dept. of Neurology,
DMCH, Ludhiana.

Dr. Pavneet Kaur Selhi
Prof.,
Dept. of Pathology,
DMCH, Ludhiana.

The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

S P Singh

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

59. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
60. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

SPECTRUM AND OUTCOME IN ADULT PATIENTS OF SUBACUTE AND CHRONIC MENINGITIS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED

IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

DOCTOR OF MEDICINE

IN

MEDICINE

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

March 2021

DR. SHIVIKA

DEPARTMENT OF MEDICINE
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	**SPECTRUM AND OUTCOME IN ADULT PATIENTS OF SUBACUTE AND CHRONIC MENINGITIS**
For the degree of	**M.D MEDICINE**
Name of the candidate	**Dr. Shivika**
Supervisor	Dr. Gautam Ahluwalia, Professor, Department of Medicine, DMCH, Ludhiana
Co-supervisor	Dr. Gagandeep Singh, Professor & Head, Department of Neurology, DMCH, Ludhiana Dr. Pavneet Kaur Selhi, Professor, Department of Pathology, DMCH, Ludhiana.
Institution	Dayanand Medical College & Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

INTRODUCTION: Meningitis is defined as inflammation involving the meninges of the brain and spinal cord. Meningitis can be categorized as acute, subacute, or chronic based on duration of inflammation. Chronic meningitis affects about 10% of patients diagnosed with meningitis. Some individuals with chronic meningitis seek medical attention before the symptoms or signs have been present for 4 weeks, so it is important to differentiate these patients from those who are recovering from acute or recurrent meningitis.

AIMS & OBJECTIVES: To study the spectrum and outcome of admitted adult patients aged > 18 years with subacute and chronic meningitis.

MATERIAL & METHODS: A prospective study shall be conducted on patients aged more than 18 years admitted with subacute and chronic meningitis in Department of Medicine and allied Specialities of Dayanand Medical College and Hospital (DMCH), Ludhiana from 1st March 2021 to 28th February 2022. Those part of the study shall have to satisfy the inclusion criteria and have none of the exclusion criteria. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

CLINICAL SIGNIFICANCE: Subacute meningitis (SAM) is commonly defined as inflammation evolving for greater than 5 days and less than 30 days and chronic meningitis (CM) as greater than 30 days without resolution of cerebrospinal fluid (CSF) abnormalities. Patients with chronic meningitis usually have a subacute onset of symptoms including fever, headache, and vomiting. The symptoms can remain static, fluctuate, and/or slowly worsen. In our country, there is a paucity of epidemiological data about subacute and chronic meningitis, especially in admitted patients. This study is aimed at delineating the etiology and clinical spectrum of subacute and chronic meningitis in patients admitted in a tertiary care teaching hospital

KEYWORDS: CHRONIC MENINGITIS (CM), CEREBROSPINAL FLUID (CSF).

Candidate's sign | Co- supervisor's sign | Co- supervisor's sign | Supervisor's sign | Principal's sign

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"SPECTRUM AND OUTCOME IN ADULT PATIENTS OF SUBACUTE AND CHRONIC MENINGITIS"** exist in the Department of General Medicine, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis are genuine and is collected by the candidate himself under our supervision and guidance.

Supervisor

Dr Gautam Ahluwalia
Professor
Department of Medicine
DMCH, Ludhiana

Co-Supervisor(s)

Dr. Gagandeep Singh
Professor & Head
Department of Neurology
DMCH, Ludhiana

Dr. Pavneet Kaur Selhi
Professor
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DMCH, Ludhiana

HEAD OF DEPARTMENT

Dr. Dinesh Gupta
Professor and Head
Department of Medicine
DMCH, Ludhiana

Place: _____

Date: _____

APPROVAL PROFORMA
BY RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Shivika
Department	Medicine
Topic of Thesis	SPECTRUM AND OUTCOME IN ADULT PATIENTS OF SUBACUTE AND CHRONIC MENINGITIS
Likely date of appearing in PG examination	MAY 2023
Date of enrolment	July 2020
Name of Head of Department	Dr. Dinesh Gupta
1) Supervisor **2) Co-Supervisor**	Dr. Gautam Ahluwalia Dr. Gagandeep Singh Dr. Pavneet Kaur Selhi
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)	Dr. Sandeep Kaushal (Dean Academics & Professor & Head, Pharmacology)
Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / No

Dr. Sandeep Puri
Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT

PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	DR. SHIVIKA H NO 7, WADHWAR COLONY, NEAR DAULA GATE, GIDDERBAHA, DISTT MUKTSAR PIN- 152101
2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital, Ludhiana
3	COURSE OF STUDY AND SUBJECT	MD Medicine
4	DATE OF ADMISSION OF COURSE	26th JULY 2020
5	TITLE OF THE TOPIC	SPECTRUM AND OUTCOME IN ADULT PATIENTS OF SUB ACUTE AND CHRONIC MENINGITIS

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Meningitis is defined as inflammation involving the meninges of the brain and spinal cord. Meningitis can be categorized as acute, subacute, or chronic based on duration of inflammation. Subacute meningitis (SAM) is commonly defined as inflammation evolving for greater than 5 days and less than 30 days and chronic meningitis (CM) as greater than 30 days without resolution of cerebrospinal fluid (CSF) abnormalities. Most organisms causing acute meningitis rarely persist more than a few weeks.[1]Patients with chronic meningitis usually have a subacute onset of symptoms including fever, headache, and vomiting. The symptoms can remain static, fluctuate, and/or slowly worsen. The symptoms and clinical course of chronic meningitis vary widely from patient to patient.

Chronic meningitis affects about 10% of patients diagnosed with meningitis.[2] Some individuals with chronic meningitis seek medical attention before the symptoms or signs have been present for 4 weeks, so it is important to differentiate these patients from those who are recovering from acute or recurrent meningitis.[3]

In our country, there is a paucity of epidemiological data about subacute and chronic meningitis, especially in admitted patients. This study is aimed at delineating the etiology and clinical spectrum of subacute and chronic meningitis in adult patients admitted in a tertiary care teaching hospital.

6.2 REVIEW OF LITERATURE

Meningitis is defined as the inflammatory process of the membranes that surround the brain and spinal cord. Meningitis is also referred to as arachnoiditis or leptomeningitis. Meningitis affects the arachnoid, pia and CSF.

When the meninges, the subarachnoid space, and the brain parenchyma are all frequently involved in the inflammatory reaction it is defined as meningoencephalitis.

Zunt et al suggested that Meningitis can be categorized as acute, subacute, or chronic based on duration of inflammation. Community acquired meningitis can be classified as acute or subacute based on the duration of symptoms of < 5 or >5 days. Chronic meningitis is commonly defined as inflammation evolving during weeks to months without resolution of CSF abnormalities. Determining the time course of meningitis is important for creating a differential diagnosis. Although numerous etiologies of subacute and chronic meningitis have been identified, the most common etiologies are: (1) infectious, (2) autoimmune, and (3) neoplastic.[4]

Ginsberg et al suggested that Meningitis is a clinical syndrome characterized by inflammation of meninges. The classic triad of meningitis consists of fever, headache and neck stiffness[5] . Bacterial meningitis occurs in about 3 people per 100,000 annually in western countries. Population-wide studies have shown that viral meningitis is more common at 10.9 per 100,000[6] population.

Meningitis was initially recognized in the early 1800's. Even until the beginning of 20th century bacterial meningitis was nearly 90% fatal. This shows that the disease is most virulent and causes a great deal of mortality and morbidity. The advent of the antibiotics in the beginning of the twentieth century brought a cure to meningitis. Inspite of antibiotics the sequelae of meningitis after completion of treatment is a great burden to the society.[7]

Bacterial (pyogenic) meningitis is a pyogenic inflammation of meninges and subarachnoid cerebrospinal fluid (CSF) and is characterized by neutrophilic pleocytosis in CSF.[7] Pneumococcal meningitis is caused

by streptococcus pneumonia, a gram positive coccus and is the most common bacterial cause of meningitis. Meningococcal meningitis is caused by gram-negative diplococcus - Neisseria meningitides. Most patients recover completely if appropriate antibiotic therapy is instituted promptly.[8]

Tubercular meningitis is a very critical disease in terms of fatal outcome and permanent sequelae, requiring rapid diagnosis and treatment.[9] Tuberculous meningitis should be a strong consideration when a patient presents with clinical picture of meningoencephalitis, especially in high risk groups, including persons with malnutrition, those with abuse alcohol or drugs and patients with known retroviral infection. Death may occur as a result of missed diagnosis and delayed treatment.[10]

Two commonly used methods -Thwaites' scoring system (Table 1)[11], and more recently, the Lancet consensus scoring system (Table 2) have been developed to help determine the probability of TBM and to help clinicians determine if TBM should be suspected and empirically treated.[12] The scoring systems include clinical features, CSF findings, as well as neurological imaging in making a diagnosis. This study was designed to explore the diagnostic utility of the "Thwaites' system" and "Lancet consensus scoring system" in differentiating TBM from the othermore common etiologies of SAM where TBM is an important consideration.

Table 1 Thwaites scoring system

	Score
Age (years)	
≥ 36	2
< 36	0
WBC (10^3 /ml)	
≥ 15,000	4
< 15,000	0
History of illness (days)	
≥ 6	5

< 6	0
CSF total WBC (10^3 /ml)	
≥ 900	3
< 900	0
CSF % neutrophils	
≥ 75	4
< 75	0

Table 2 Lancet scoring system	
Clinical criteria Score	**(Maximum category score = 6)**
Symptom duration of more than 5 days	4
Systemic symptoms suggestive of tuberculosis	
(one or more of the following): weight loss	2
(or poor weight gain in children), night sweats	
, or persistent cough for more than 2 weeks	
History of recent (within past year) close contact	
with an individual with pulmonary tuberculosis	2
or a positive TST or IGRA (only in children < 10 years of age)	
Focal neurological deficit (excluding cranial nerve palsies)	1
Cranial nerve palsy	1
Altered consciousness	1
CSF criteria	**(Maximum category score = 4)**
Clear appearance	1
Cells: 10–500 per µl	1
Lymphocytic predominance (> 50%)	1
Protein concentration greater than 1 g/L	1
CSF to plasma glucose ratio of less than 50% or	
an absolute CSF glucose concentration less	1
than 2·2 mmol/L	
Cerebral imaging criteria	**(Maximum category score = 6)**
Hydrocephalus	1
Basal meningeal enhancement	2
Tuberculoma	2
Infarct	1

Pre-contrast basal hyperdensity	2
Evidence of tuberculosis elsewhere (Maximum category score = 4)	
signs of tuberculosis = 2; miliary tuberculosis = 4	2/4
CT/ MRI/ ultrasound evidence for tuberculosis outside the CNS	2
AFB identified or Mycobacterium tuberculosis cultured	
from another source—i.e., sputum lymph node,	4
Positive commercial M tuberculosis NAAT from extra-neural specimen	4

Exclusion of alternative diagnoses

An alternative diagnosis must be confirmed microbiologically (by stain, culture, or NAAT when appropriate), serologically (eg, syphilis), or histopathologically (eg, lymphoma). The list of alternative diagnoses that should be considered, dependent upon age, immune status, and geographical region, include: pyogenic bacterial meningitis, cryptococcal meningitis, syphilitic meningitis, viral meningo-encephalitis, cerebral malaria, parasitic or eosinophilic meningitis (Angiostrongylus cantonesis, Gnathostomaspinigerum, toxocariasis, cysticercosis), cerebral toxoplasmosis and bacterial brain abscess (space-occupying lesion on cerebral imaging)and malignancy (eg, lymphoma)

TST tuberculin skin test, IGRA interferon-gamma release assay, NAAT nucleic acid amplification test, AFB acid-fast bacilli. The individual points for each criterion(one, two, or four points) were determined by consensus and by considering their quantified diagnostic value as defined in studies

The “Thwaites’ system” and “Lancet consensus scoring system” showed poor diagnostic accuracy to distinguish TBM from other causes of SAM and CM. Other etiologies should be considered especially in patients with possible TBM by Lancet criteria. Novel CSF molecular diagnostic methods may increase the yield to identify the etiologies and ultimately improve care.[1]

TBM is a medical emergency associated with high morbidity and mortality. Early empirical treatment with ATT should be started if clinical suspicion is high. Ensuring compliance with chosen ATT regimen and supportive therapy cannot be overemphasized. Current ATT regimens are extrapolated from PTB regimens and do not consider poor CNS penetration of drugs such as ethambutol, streptomycin, and rifampicin. Improvement in social indicators of a country, namely, malnutrition, poverty, and low income will play an important role in the prevention and control of TB.[13]

World-wide causes of viral meningitis include enterovirus, herpes, mumps, measles and HIV. Enterovirus is the most common cause of viral meningitis. Aseptic meningitis is an illness characterized by serious inflammation of the meninges, usually with an accompanying CSF lymphocyte pleocytosis. Clinical manifestations vary with headache and fever predominating. The illness is usually mild and runs its course without treatment, however some cases can be severe and life threatening. Remarkable recovery may be achieved in some patients with viral meningitis who become even comatosed. Vigorous supportive therapy and avoidance of complications are very important in managing these patients.[14]

Cryptococcal meningitis is caused by the yeast Cryptococcus neoformans, especially in persons with defective cell mediated immunity. Prompt antifungal therapy should be considered in these patients. [15]

The incidence of acute encephalitis in western countries is 7.4 per 100,000 populations per year. In tropical countries like India it is 6.4 per 100,000 per year. Encephalitis presents as diffuse or focal neuropsychological dysfunction although it primarily involves the brain, it often involves the meninges as well (meningo encephalitis). From an epidemiologic and pathophysiologic perspective encephalitis is distinct from meningitis, though on clinical evaluation both can be present, with signs and symptoms of meningeal inflammation. The prodome typically consists of fever, headache, nausea, vomiting, lethargy and myalgias. The clinical presentation is encephalopathy with diffuse or focal

neurological symptoms including behavioural and personality changes, with decreased level of consciousness, neck pain/stiffness, photophobia, lethargy, generalized or focal seizures, acute confusion or amnestic states and flaccid paralysis.[16]

Distinguishing the etiologies also helps in terms of both reducing antibiotic usage and hospital bed occupancy and reassuring contacts of cases and health care staff of a non-bacterial causes. This study is done to emphasize the importance of early diagnosis, so that prompt management is given at appropriate time.

6.3 AIMS AND OBJECTIVES OF THE STUDY

To study the spectrum of admitted adult patients aged > 18 years with subacute and chronic meningitis .

To study the outcome in these patients; wherever feasible

7.0 MATERIALS AND METHODS

7.1 SOURCE OF DATA

All the patients aged more than 18 years admitted with subacute and chronic meningitis in Department of Medicine and allied Specialties of Dayanand Medical College and Hospital (DMCH), Ludhiana

7.2 METHOD OF COLLECTION OF DATA

Study Population

A prospective observational study will be conducted in adults patients hospitalized with subacute and chronic meningitis in DMCH, Ludhiana. This study duration will be from 1st March 2021 to 28th February 2022.

Inclusion Criteria

- Age $\geq$ 18 years.
- Patients with symptoms of subacute and chronic meningitis admitted in department of Medicine and allied specialties.
- Duration of symptom more than 5 days
- CSF White cell count > 5 cells/mm^3

Exclusion Criteria

- Age < 18 years.
- Previous history of trauma or with cerebrospinal fluid leak or any previous history of neurosurgery.
- Patients not giving consent for enrollment in the study.

OUTCOME

- Diagnosis at time of discharge / discharge on request (DOR) / death / discharge against medical advice (DAMA).
- Length of stay in hospital.
- Clinical/laboratory/treatment profile of admitted patients.
- Details of pre admission workup and treatment outside(wherever available)
- Follow-up post-discharge (wherever feasible) Months: 2 and 4

Statistical Analysis:

The data will be analyzed statistically using appropriate methodology. Data will be described in terms of range; mean ±standard deviation (±

SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations will be done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Investigations considered necessary by the treating unit/ department will be evaluated. The investigations will be broadly divided into the following groups:

- Basic investigations: CBC, LFT, RFT, Urine routine, inflammatory markers like ESR
- Specific investigations: cerebrospinal fluid analysis - biochemical and/or cytopathological analysis and/or nucleic acid amplification test and/or gram stain and/or culture and/or India ink and/or viral markers and/or autoimmune antibodies.
- Radiological investigations: Chest X-Ray, CT Scan, MRI
- Detailed proforma format is attached herewith with thesis plan

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Yes Attached herewith

LIST OF REFERENCES

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16. Bloch KC, Glaser C. Diagnostic approaches for patients with suspected encephalitis. Curr Infect Dis Rep. 2007;9:315-22.

PROFORMA

S. No.

Name Age Gender

Date of admission Date of discharge

Mrd Number Admission no.

Ward/Unit

Address

Mobile no.

Outcome of the patient-Discharge/Death/Dama/Discharge on request

Outcome diagnosis

Length of stay

In ward Days

In ICU Days

Chief complaints at the time of admission

CNS SYMPTOMS

Altered Sensorium

Duration

Fever

Duration

Continuous/Intermittent

Chills/Rigors

Evening Rise

Headache

Duration

Time of headache

Site

Stiff neck

Photophobia

Seizures

Type

Duration of seizure

Malaise

Signature of Candidate **Signature of Co-Supervisor** **Signature of Supervisor**

RESPIRATORY SYMPTOMS

Cough

Dry/Expectoration

Dyspnea

Grade

ABDOMINAL SYMPTOMS

Nausea

Vomiting

Projectile/Non Projectile

Frequency

Pain Abdomen

GENITOURINARY SYMPTOMS

Burning Micturition

Increased Frequency of Micturition

Decreased Urine Output

Others

PRESENTING SIGNS

Nuchal rigidity

Vesicular or petechial rash

Presence of altered mental status

Disorientation

Focal motor deficit

Cranial nerve abnormality

Aphasia

PAST HISTORY

Tuberculosis	Diabetes mellitus	CAD
Hypertension	CKD	CLD

Trauma

Seizure disorder

Other underlying co-morbidities

Signature of Candidate **Signature of Co-Supervisor** **Signature of Supervisor**

Surgical History

Blood Transfusion

PERSONAL HISTORY

Vegetarian/Non-vegetarian

Smoker/Non-smoker: Duration

Quantity

Alcoholic/Non-alcoholic: Duration

Quantity

Menstrual history- Regular

Amount of flow

Substance Abuse

DRUG HISTORY

Anti-Epileptic

Anti-Tubercular

Anti-Psychotic

Others

General physical examination

Appearance	Sensorium	
Pallor	Icterus	Cyanosis
Clubbing	Edema: Pitting/non-pitting	
Skin: Rash	Type of Rash	
LAP		
Trachea	JVP	

Signature of Candidate **Signature of Co-Supervisor** **Signature of Supervisor**

VITALS

Temperature	SBP	DBP
Pulse	RR	Glasgow coma score
Pupil size	Pupil reaction	

Nutritional Assessment

Body Weight	Height	BMI

Systemic examination

CNS

MENINGITIC SIGNS

Neck rigidity

Kernig's sign

Brudzinski sign

HIGHER MENTAL FUNCTIONS

Level of consciousness

Orientation to Time

Place

Person

CRANIAL NERVE EXAMINATION

MOTOR EXAMINATION

REFLEXES

Deep tendon reflexes

Superficial reflex

SENSORY EXAMINATION

CEREBELLAR SIGNS

FUNDUS EXAMINATION

RESPIRATORY

P/A

CVS

Signature of Candidate **Signature of Co-Supervisor** **Signature of Supervisor**

Investigations

Parameters	At admission	At discharge
Hemogram		
Hb		
MCV		
TLG		
DLC		
Platelet		
ESR		
PBF		
LFT		
Total bilirubin		
Direct bilirubin		
SGOT		
SGPT		
ALP		
Total protein		
Serum Albumin		
A:G ratio INR/PT		
RFT		
Blood urea		
Serum Creatinine		
Serum Electrolyte Na/K/Cl		
Ca/Mg/Phosphorus		
Uric acid		
CRP		
Viral markers **AntiHIV**(Rapid/ELISA)		
  AntiHCV(Rapid/ELISA)		
  HbSAg(Rapid/ELISA)		
Mantoux test – Induration Size		

Signature of Candidate **Signature of Co-Supervisor** **Signature of Supervisor**

Blood culture and sensitivity

Urine culture and sensitivity

Specific investigations

CEREBROSPINAL FLUID ANALYSIS

Parameters	Value
Gross	
Ph	
BIOCHEMISTRY: Fluid protein Fluid glucose Fluid chloride	
PATHOLOGY Total Cell Count Differential Cell Count • MNC • Neutrophil	
MICROBIOLOGY GRAM STAIN CULTURE	
CBNAAT	
ADA	
CRYPTOCOCCAL	
HSV	
CULTURE	
MALIGNANT CELLS	
AUTOIMMUNE	

CHEST X RAY Findings

CT Findings

MRI Findings

EEG

OUTSIDE REPORTS

ANY OTHER INVESTIGATIONS

Signature of Candidate **Signature of Co-Supervisor** **Signature of Supervisor**

FOLLOW UP

2 MONTHS/ 4 MONTHS

DATE:

CONSTITUTIONAL FEATURES

FEVER- YES / NO

IF NO -DATE OF SUBSIDENCE OF FEVER

NAUSEA- YES/ NO

VOMITING- YES / NO

HEADACHE- YES/ NO

ANY FOCAL NEUROLOGICAL DEFICIT- YES/ NO

IF YES- NEW ONSET/ PREVIOUS

SIDE EFFECTS OF DRUGS-

HEPATITIS

NAUSEA AND VOMITING

SKIN RASH

ANY OTHER SIDE EFFECT

DID SIDE EFFECTS LEAD TO DISCONTINUATION OF DRUGS

CHANGE IN MEDICATION PLAN

INVESTIGATIONS:

ESR

REPEAT IMAGING

(CT/MRI)

FINAL OUTCOME: IMPROVED CLINICALLY / IMPROVED PARTIALLY/WORSENED

Signature of Candidate **Signature of Co-Supervisor** **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....
.....am willing to participate in the study **"SPECTRUM AND OUTCOME IN ADULT PATIENTS OF SUBACUTE AND CHRONIC MENINGITIS "** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

.....
Signature of the Witness

.....
Signature of the patient

Name:

Signature of Candidate

Signature of Supervisor

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____

निवासी _____

इस शोधकार्य **"SPECTRUM AND OUTCOME IN ADULT PATIENTS OF SUBACUTE AND CHRONIC MENINGITIS "** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"SPECTRUM AND OUTCOME IN ADULT PATIENTS OF SUBACUTE AND CHRONIC MENINGITIS" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ